November/December 2022. Vol 89 No 6
SA Pharmaceutical Journal
sapj
ISSN: 2221-5875

NEW TussMuco

N-acetylcysteine 200 mg / tablet

Dear Healthcare Professional,

Re: TUSSMUCO Launch

Aspen is excited to launch new TUSSMUCO 200 mg Effervescent Tablet in 15s and 25s packs.

TUSSMUCO is indicated as a mucolytic of non-infective secretions in cystic fibrosis and in respiratory conditions and is available from your regular wholesaler.

Product description	Dose form	Pack size	NAPPI code	S.E.P. (excl. VAT)	S.E.P. (incl. VAT)
TUSSMUCO	200 mg Effervescent Tablet	15 Tabs	3003379001	R38,49	R44,26
TUSSMUCO	200 mg Effervescent Tablet	25 Tabs	3003379002	R64.15	R73,77

Provides a 20 % cost saving vs the market leader [1]

For further information, please contact me directly on +27 11 239 3580, or our Customer Care Line on 0800 122 912.

Regards,

Karen Liddle
Brand Manager
Aspen Pharmacare
Healthcare Park, Woodlands Drive, Woodmead, 2191
Direct Tel.: + 27 11 239 3580 Email: KLiddle@aspenpharma.com

Reference 1: Medikredit Manufacturing Pricing Report April 2022

Healthcare. We Care.

aspen PHARMACARE

Marketed by Aspen Pharmacare
www.aspenpharma.com
Medical Hotline 0800 118 088

sapj

SA Pharmaceutical Journal

Official journal of the

Pharmaceutical Society of SA
incorporating
- Academy of Pharmaceutical Sciences
- South African Association of Community Pharmacist Sector of the PSSA
- SA Association of Hospital and Institutional Pharmacists
- SA Association of Pharmacists in Industry

www.sapj.co.za

ISSN: 2221-5875

ADVERTISING SALES
Sandy Whitehouse (Medpharm)
Cell: 082 853 4155
E-mail: sandy@medpharm.co.za

SUBSCRIPTION
info@medpharm.co.za

PUBLISHER
The Pharmaceutical Society of South Africa in collaboration with
Medical & Pharmaceutical Publications (Pty) Ltd
trading as Medpharm Publications
Registration No 93/0794007

The Pharmaceutical Society of South Africa,
435 Flinders Avenue, Lynnwood, 0081
PO Box 75769, Lynwood Ridge, 0040
Tel: (012) 470 9550, Fax: (012) 470 9556
www.pssa.org.za
E-mail: nitsa@pssa.org.za

Medpharm Publications,
Ground Floor, Centurion Wine & Art Centre,
123 Amkor Road, Lyttelton Manor
PO Box 14804, Lyttelton, 0157
Tel: (012) 664-7460, Fax: (012) 664-6276
E-mail: info@medpharm.co.za
www.medpharm.co.za

BusinessPrint
meeting expectations

contents

SAPJ Author Guidelines

Thank you for choosing SAPJ in which to publish your paper.

Aims, scope and review policy

SAPJ is aimed at the continuing professional development of the South African pharmacist in a variety of practice settings, including clinical pharmaceutical care practitioners in a community or hospital pharmacy environment, and pharmacists in academic and industrial practice.

The journal accepts specific clinical reviews on self-medication topics (symptomatic therapy) and information on prescription medication (therapy in clinical context), and provides pharmacists with essential information for referring customers for early medical attention should it be required. SAPJ further recognises that the role of the pharmacist continually evolves to meet the needs of the population. An example of this is the provision of accessible, basic primary health care services in community pharmacies.

Papers dealing with medicines safety issues, including the safe and appropriate prescription, administration and use of medication as well as pharmacovigilance, are strongly advocated in SAPJ. SAPJ further supports pharmacists in transforming the pharmacy into an accessible, basic primary health care facility for preventing and treating primary health care conditions through diagnosis, screening and treatment.

The journal is currently indexed by Google Scholar via www.sapj.co.za and enjoys wide international exposure. An 'electronic long, paper short' policy will be followed for original papers where abstracts of original papers are featured in the printed copy with the full version available online.

Online submission

All articles must now be submitted online at www.sapj.co.za

The electronic submission process will prompt you to check off the following declarations:

1. This manuscript has currently only been submitted to SAPJ and has not been published previously.
2. This work is original and all third party contributions (images, ideas and results) have been duly attributed to the originator(s).
3. Permission to publish licensed material (tables, figures, graphs) has been obtained and the letter of approval and proof of payment for royalties have been submitted as supplementary files.
4. The submitting/corresponding author is duly authorised to herewith assign copyright to Medical and Pharmaceutical Publications (Pty) Ltd
5. All co-authors have made significant contributions to the manuscript to qualify as co-authors.
6. Ethics committee approval has been obtained for original studies and is clearly stated in the methodology.
7. A conflict of interest statement has been included where appropriate.
8. A title page has been uploaded as a separate supplementary file and the submission adheres to the instructions to authors in terms of all technical aspects of the manuscript.

How to submit your paper online:

1. Visit www.sapj.co.za.
2. Register with the website as an author and log in.
   - Click on LOG IN and log in with username and password if already registered.
   - If you have forgotten your password: Click on Forgot your password?
   - If you are not registered, click on: Not a user? Register with this site.
3. Select Author.
4. Click on CLICK HERE TO FOLLOW THE FIVE STEPS TO SUBMIT YOUR MANUSCRIPT .
5. Follow the five steps to submit your paper.

Article sections and length

The following contributions are accepted (word counts include abstracts, tables and references):

Original research:	3 200–4 000 words
Evidence- based pharmacy practice:	3 200–4 000 words
Reviews:	2 400–3 200 words
Case studies:	1 800 words
Scientific letters:	1 200–1 800 words
Letters to the editor:	400–800 words

For a full version of the SAPJ author guidelines, please visit www.sapj.co.za

peploc

PANTOPRAZOLE 20 mg, 40 mg

- Low Potential Drug Interaction[1]
- Max plasma concentration of 40 mg, 2,5 h after administration[2]

For further product information contact **PHARMA DYNAMICS**
Email info@pharmadynamics.co.za **CUSTOMER CARE LINE** 0860 PHARMA (742 762)

PEPLOC 20, 40 mg. Each tablet contains pantoprazole sodium sesquihydrate equivalent to Pantoprazole 20, 40 mg respectively. S4 A42/11.4.3/0056, 0057 NAM NS2 10/11.4.3/0473, 0474. For full prescribing information, refer to the professional information approved by SAHPRA, 2 August 2021. 1.Wedemeyer RS, *et al.* Pharmacokinetic Drug Interaction Profiles of PPIs: An Update. Drug Saf 2014;37"201-211. 2. Peploc Package Insert. **PCOA/668/08/2022**

pharma dynamics
EFFECTIVE AFFORDABLE HEALTHCARE

www.pharmadynamics.co.za

A Piece of my Mind

Editorial Comment

Sometimes work is fun, sometimes it's a nightmare, and most of the time it's same old, same old. Have you found that too?

I must say that the *SAPJ* suits me well. Don't tell anyone (I'll deny it if you do) but clearly I'm a busybody – I love hearing about where everyone else's work journey is taking them.

Changes in leadership

May I be (one of the) first to congratulate Kaajal Chetty on her new job as the Director of the PSSA's Western Cape Branch. And may I give you a word of advice, Kaajal? If anyone gives you lip, just set Gary Black on them! His rugby background makes him a very useful strategic and physical ally! (And his choice of wine at dinner one evening was based on which ex-rugby player owned the vineyard. That was extremely useful to know.) By the way, Gary, please remind Kaajal that working for the PSSA increases her obligation to write for me – it doesn't decrease it. And while you're at it, isn't it time to devote more time to your Little Black Book? (And so sorry, Dr KK Naidoo, newly appointed director of the KZN Coastal branch of the PSSA, I was so excited to see you at the PSSA conference that I forgot to remind you to write to me!)

New leadership at SAAHIP

You'll hear from and about them soon, but obviously with Kaajal moving to the CWP branch of the PSSA, it was necessary to elect a new SAAHIP presidential committee for the remainder of the current term of office. Congratulations to the newly elected members – president Nhlanhla Mafarafara (affectionately known as Faraz), vice president Obey Madzingo and secretary Armand Algra. Hannes Stegmann continues as treasurer. So an all-male presidential committee, but there are enough women around to keep an eye on them!

Well done, Keith and Gawie

And I was interested to hear that Geard Pharmacy, with stalwart Keith Johnson and not such a newbie but still young Gawie Malan, won the award in the recent Malmesbury Business Chamber for the category best medium-sized business. Well done, lads.

New leadership parameters

Someone else who inspired me this month is Tlou Mauvis Moloto-Shivambu. Older people (like me) have always understood the abbreviation to KPI to refer to Key Performance Indicators. Mauvis posted on Facebook (or stalkbook, as Briony Chisholm refers to it) that the new leadership uses KPI as meaning:

- Keep people interested
- Keep people informed
- Keep people involved
- Keep people inspired

Doesn't that sound what we'd appreciate from our leaders? Are they living up to this? Should we not be demanding it? Or at least gently encouraging our leaders to offer it?

Changes in pharmacy's focus

When I graduated as a pharmacist, at the end of 1980, I hadn't heard of primary health care, even though the World Health Organization (WHO) conference on primary health care had adopted the Alma-Ata Declaration in 1978.

Look at us now – 44 years later, there isn't (or shouldn't be) a pharmacy graduate who doesn't understand the principles of primary health care. This was updated in 2018 by the Astana Declaration on Primary Health Care (PHC), for which the International Pharmaceutical Federation (FIP) pledged its commitment to accelerate progress in strengthening PHC. In 2020, the WHO published its Operational Framework for PHC to translate the vision of the Astana Declaration into actions.

And isn't it wonderful – FIP recently held a global summit on primary health care, with the focus "Pharmacists transforming vision into action". The PSSA was privileged to be represented by its Deputy President, Refiloe Mogale. Well done, Refiloe. You did us proud!

And by the way, if you get bored with websites and don't enjoy going to official websites, try FIP's Facebook page for a bird's eye view of their activities – very enlightening!

Lorraine Osman

President's Message

Opportunities for personal and professional growth

Joggie Hattingh
PSSA President

Dear colleagues and friends

I have been extremely blessed to have had the opportunity to attend many conferences over the past two decades. These were opportunities to meet new people, to build relationships and networks and to foster new friendships, and also to expand my views, share best practice and learn what is topical and interesting in my field of practice.

There were many PSSA, SAAHIP, SAACP and Academy conferences and although as President of PSSA I was an invited guest to most conferences during my tenure, none comes without personal sacrifices, costs and contributions.

I was privileged to attend the FIP Conference 2022 in Seville, Spain where FIP treated us to a wide array of presentations, panel discussions, poster presentations and plenary sessions. With the parallel sessions, everyone had the opportunity to attend sessions that was of interest to them, and every sector of the profession was catered for.

It has become custom for the South African delegation (around 22 individuals on this occasion) to spend an evening together around a dinner table, where we get to know each other. This year it was at a tapas restaurant on the sidewalk in Seville! It was an experience to remember and to savour long afterwards.

I was honoured to participate in a lunch-hour panel discussion that was organised by The General Pharmaceutical Council of Spain and chaired by our own Dr Sham Moodley. The topic was ***'Empowering pharmacy-based self-care with health literacy'***.

This is such an important, but often neglected topic, as health literacy has a direct correlation with health outcomes and GDP. So, to improve general health and increase our GDP, we need to improve our population's health literacy! Should health literacy not then be included in the curriculum of all learners at an age-appropriate level, from primary school onwards?

One statement that was made during the opening session and stayed with me, was that spending on health personnel is not a burden on the economy. It is an investment that will directly impact the GDP of the country as health outcomes improve.

Another topic that was seen throughout the conference was that pharmacists across the globe, not only stepped in during the COVID-19 pandemic and ensured that patients continued to receive their medicine, but also stepped up, to help render vaccinations, to ensure stock shortages were mitigated and managed appropriately. This happened while many doctors closed their doors and only consulted patients per telephone or virtually!

From this it became clear that we need to utilise our pharmacists better to ensure access to primary healthcare and the need to integrate private pharmacies into the primary healthcare system, was highlighted. We also need to formalise the roles and functions pharmacists could fulfil during a public health crisis whilst planning for future public healthcare emergencies.

We have stepped up and shown the value we bring to healthcare internationally! Now we need to consolidate our position and not allow pharmacy to be side-lined once the dust has settled on the COVID-19 pandemic.

There are many local conferences organised by the PSSA and the sectors of the PSSA that are inexpensive to attend. I urge all pharmacists to start planning their attendance in advance. If this is not done, one often realises that the opportunity has come and gone whilst one was focusing on other matters.

To all my colleagues and friends, please make an effort to attend a FIP conference. Next year it will be held in Brisbane, Australia, but the year after (in 2024), it will be in Cape Town. No excuses!

Leading the way in African Pharmaceutical Sciences to produce 21st-century medicines

Congratulations to Professor Yahya Choonara (https://orcid.org/0000-0002-3889-1529), who recently received a leading international accolade recognising his outstanding research and significant contributions to the Pharmaceutical Sciences globally.

The Bureau of the International Pharmaceutical Federation (FIP) (https://www.fip.org/who-we-are) selected him for the 2022 FIP Distinguished Pharmaceutical Science Award conferred at the 80th FIP World Congress of Pharmacy and Pharmaceutical Sciences held recently in Seville, Spain. The FIP represents over 4 million pharmacists and pharmaceutical scientists around the world.

As an advocate of pharmaceutical innovation, Prof. Choonara's persistent leadership in the Pharmaceutical Sciences on the continent is making an impact to global health and at the forefront of producing advanced life-saving 21st-century medicines for infectious, hereditary and lifestyle diseases.

He leads the University of the Witwatersrand's (Wits) Advanced Drug Delivery Platform (WADDP) Research Unit (https://www.wits.ac.za/waddp), a flagship unit of Wits University and Africa's first, largest and only entity in the domain contributing to the design of novel targeted drug (and/or bioactive) delivery systems, nanomedicine, functional biomaterials and regenerative medicines. Drug delivery science is the method and process of formulating a newly discovered (or existing) drug (or bioactive) to achieve a better therapeutic effect in the human body (i.e. improved bioavailability).

The development of brand new drug molecules that form part of sophisticated drug discovery programmes is relatively expensive, time consuming and comes with a very high risk of failure especially for LMICs. Hence, improving the safety-to-efficacy ratio of promising new/existing drugs by using novel methods of drug delivery (administration) can enhance, individualise and revolutionise drug therapy. This is where innovations at the WADDP are changing conformist thinking and pursued vigorously by Prof. Choonara's scientific team leading to many breakthroughs.

As a Personal Professor of Pharmaceutical Sciences, a Tier 1 South African National Research Foundation (NRF) Chair in "Pharmaceutical Biomaterials and Polymer-Engineered Drug Delivery Technologies" he holds the largest pharmaceutical product patent portfolio (43 in total) aimed at providing patient-centric drug therapies for unmet therapeutic needs including special populations (e.g. neuroscience, oncology, infectious diseases, paediatrics, women and child health). His inventions include a WaferMat (the world's fastest dissolving matrix), a VagiTab, Nanomedicine and BioInspired NeuroTherapeutics.

Prof. Yahya Choonara receiving his FIP Award

He is also the first South African Pharmaceutical Scientist and Pharmacist to receive both this FIP Award and the Department of Science and Innovation (DSI) of South Africa Top Intellectual Property (IP) Creator Award, one of the country's highest awards for distinguished contributions to innovation.

As an African Pharmaceutical Scientist, he is also very passionate on developing the next generation of Pharmaceutical Scientists for South Africa and the continent and has graduated more than 110 postgraduates and mentored more than 18 postdoctoral fellows from nine countries. He currently mentors several emerging pharmaceutical scientists at various academic institutions in South Africa and on the continent pursuing a career in pharmaceutical product development (including nanomedicine). In relation to this, he was invited to co-author two UNESCO UniTWIN inaugural reports on 'A needs-based Pharmaceutical Sciences education in Africa' and 'Addressing equitable, inclusive and quality Pharmaceutical Science education'.

PSSA Conference 2022

The PSSA finally hosted its first in-person conference since 2018 at the Indaba Hotel and Conference Centre in Fourways, Gauteng, from 1 to 3 September 2022.

When discussions about having a conference commenced, there was still uncertainty in terms of COVID-19 restrictions and whether or not it would be possible. It all worked out however, and the PSSA was able to host a successful in-person conference!

Celebrating 76 years of serving the profession

The PSSA was founded in 1946. During the past 76 years, the pharmacy profession has faced many challenges. The profession has however remained resilient and, to a large extent, has been able to turn many threats into opportunities. The latest immense challenge to the profession (and to many other professions) has been the COVID-19 pandemic. As we emerge from the worst of the pandemic, stronger and more focused, we are ready to move forward to find innovative solutions to the healthcare challenges we face in South Africa.

It was invigorating to be able to see our colleagues in person again and the discussions ranged from very deep to very passionate, and included light and humorous interludes.

The conference's academic programme was outstanding, with speakers of high-quality presenting on a wide range of topics. It was also really encouraging to see so many of the young (and the maybe not that young) pharmacists attending the conference and taking part in discussions and asking insightful questions. It was also comforting to have some of the stalwarts around, albeit with some sadness for all those we have lost over the last few years.

The main topics discussed were the following:

- PSSA – at your service for 75 years (and counting)
- Surviving the pandemic
- Legally challenged – where to from here?
- Pharmacists' role in evidence-based medicine
- Digitalisation in pharmacy
- Vaccines from Africa for Africa
- Registration of medicines in South Africa
- Mentorship in the pharmacy profession
- Pharmacy roles extended – the new faces of pharmacy

The social functions allowed for some much needed catch-up after the last two and a half years. The Fellows had a lovely Fellows dinner and welcomed the new Fellows in their midst. Fellowship certificates were formally presented to two new Fellows, Sham Moodley and Joggie Hattingh, at the Gala dinner. Fellowship was also awarded posthumously to Lee Baker. Jackie van Schoor received the award on behalf of the Baker family.

Ivan Kotzé, Executive Director, and Joggie Hattingh, President

At the conference, the PSSA held its 77th AGM and the new PSSA National Executive Committee (NEC) was appointed. The Committee was announced at the gala dinner. It was the first time that the current President was inaugurated in person and not virtually, although this is not his first term of office as President. The committee consists of:

Presidential Committee

- Joggie Hattingh – President
- Refiloe Mogale – Deputy President
- Lynette Terblanche – Honorary Treasurer
- Stéphan Möller – Immediate Past President
- Nhlanhla Mafarafara – Vice-President SAAHIP
- Gina Partridge – Vice-President SAAPI
- Johannes Ravele – Vice-President SAACP

Note: The Vice-President representing the Academy of Pharmaceutical Sciences (APSSA) will be announced shortly.

Appointed NEC members

- Morné Adamson – Pretoria Branch
- Kristi Clayton – Border and Eastern Districts Branch
- Renier Coetzee – Cape Western Province Branch
- Carrie de Beer – Cape Western Province Branch
- Rashmi Gosai – Southern Gauteng Branch
- Terry Higginson – KZN Inland Branch
- Jameel Kariem – Cape Western Province Branch
- Murial Kopanye – Pretoria Branch

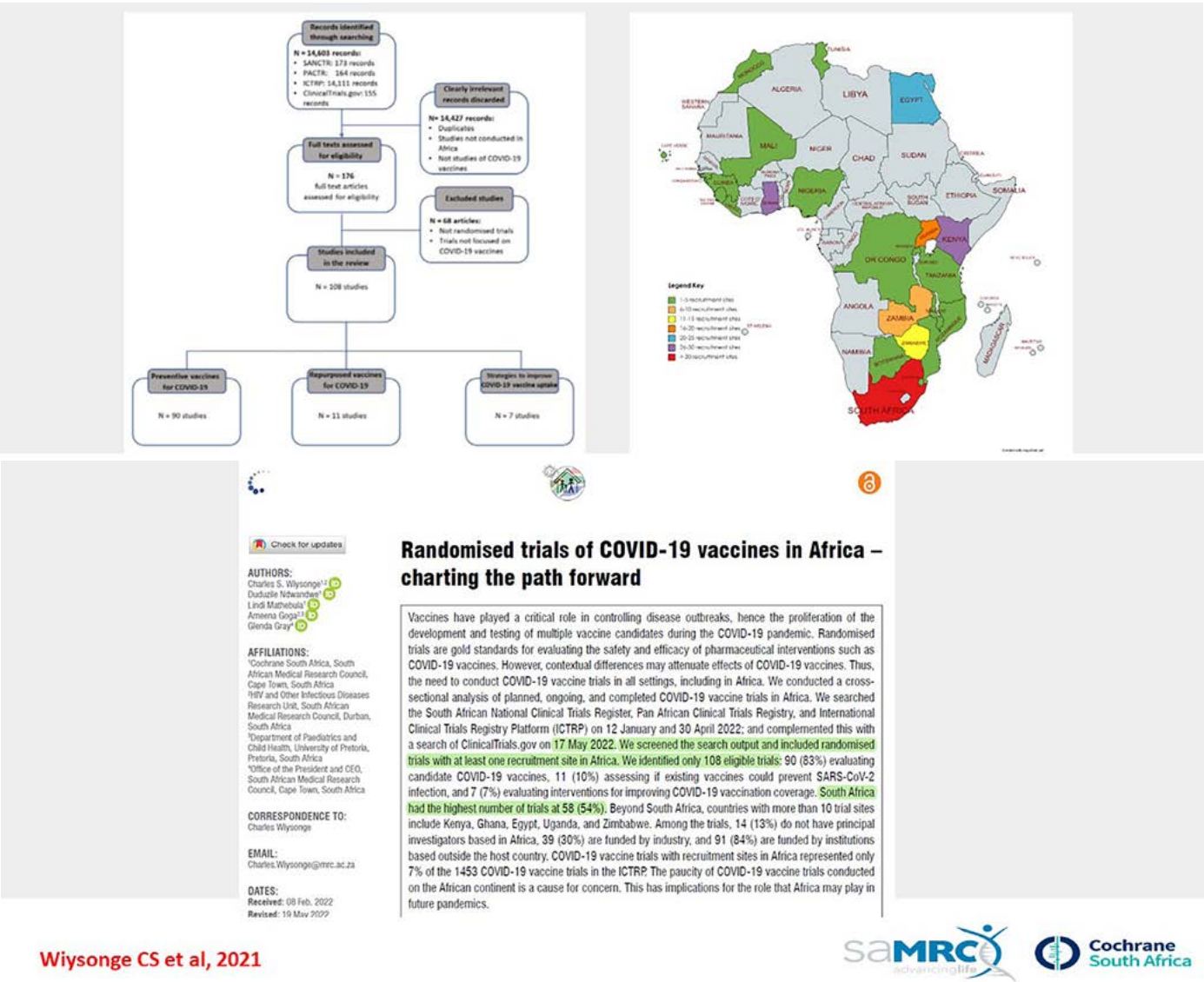
- Alice Lategan – Cape Midlands Branch
- Nelson Mabusela – YPG/Limpopo Branch
- Gawie Malan – Cape Western Province Branch
- James Meakings – Southern Gauteng Branch
- Martlie Mocke-Richter – Free State Branch
- Des Moodley – KZN Coastal Branch
- Thandeka Njapha – KZN Coastal Branch
- Thanushya Pillaye – Southern Gauteng Branch
- Nico Scheepers – North West Branch
- Mohale Seepe – Limpopo Branch
- Gideon Vosloo – Mpumalanga Branch
- Alex Wehmeyer – Cape Western Province Branch
- Shawn Zeelie – Northern Cape Branch

Stavros Nicolaou and Prof. Charles Wisonge

Vaccines from Africa for Africa

Stavros Nicolaou from Aspen Pharmacare and Prof. Charles Wisonge from the South African Medical Research Council (SAMRC) presented a session on Vaccines from Africa for Africa on Friday 2 September 2022.

During the sessions Prof. Charles talked about the COVID-19 vaccine journey in South Africa. He highlighted how South Africa has been at the forefront of clinical development of the COVID-19 vaccines and how the phase 3B Sisonke trial of the J&J vaccine



South Africa has been at the forefront of clinical development of COVID-19 vaccines

David Boyce receiving the William Patterson Award

proved to be effective in protecting against moderate and severe COVID-19 as well as death in healthcare workers.

Stavros dedicated his session to David Boyce – who was a close friend and mentor of Stavros. David was a Fellow as well as an Honorary Life Member of the Pharmaceutical Society of South Africa and was a recipient of the William Patterson Award. David was a prominent innovator in the medical scheme administration arena, and a major contributor to the Society's engagements with government over the dispensing fee. David was also, for many years, a stalwart of the Names and Scheduling Committee of the then MCC.

Stavros talked about South Africa's journey during the COVID-19 pandemic, from the first meeting with President Cyril Ramaphosa at the Union buildings until 2 September 2022.

During the pandemic, it was evident that South Africa was on its own during the pandemic. No partnerships or allies of the country made any difference when South Africa was looking to purchase personal protection equipment, medical equipment, medicines or vaccines. Each time, South Africa had to turn to its own people and resources to come up with a plan.

One of the most important scenarios was when South Africa purchased the AstraZeneca vaccines with much difficulty, only to discover that the vaccine wasn't effective against the Delta variant that was prevalent in South Africa and which had caused the most devastating wave of infection in South Africa. Prof. Glenda Gray, of the SAMRC, came up with the unique plan of conducting a phase 3B trial of the J&J vaccine that was administered to healthcare workers in South Africa. This trial ended up becoming the largest phase 3B trial of a COVID-19 vaccine, and started before any emergency use authorisation and national roll-out of the vaccine in South Africa. The findings of the study also provided additional evidence that the vaccine provided protection in the HIV-positive sub-population because the study population comprised a large number of healthcare workers with HIV.

Incidentally, South African scientists were the first to perform genomic sequencing identifying the Beta and Delta variants in the world. Despite this, the country was harshly punished for these discoveries, including imposition of travel bans.

In another first, Aspen was able to secure a licence to compound, fill, finish and package the J&J vaccine in South Africa as a contract manufacturer at their sterile manufacturing plant in Gqeberha. Unfortunately initially all the vaccines they manufactured had to be returned to J&J for distribution in other countries. However in July 2021, Aspen was finally able to release some of the batches of vaccines they manufactured to South Africa. In addition, vaccines from these batches were also made available through the African Vaccine Acquisition Task Team/African Union platform. This represented a significant landmark for South Africa and the African continent as these were the first COVID-19 vaccines to be produced on the African continent, by an African producer for South African and African patients.

Due to funding difficulties in other African countries and a low demand in South Africa, the number of batches of COVID-19 vaccine manufactured at the Gqeberha plant has reduced dramatically, leaving capacity for other vaccines to be manufactured. Aspen recently announced that they have concluded a ten-year agreement with the Serum Institute of India (the world's largest vaccine manufacturer) to manufacture, market and distribute four Aspen-branded routine vaccines in Africa, namely Pneumococcal Vaccine, Rotavirus Vaccine, Polyvalent Meningococcal Vaccine and Hexavalent Vaccine.

One of the lessons that Africa has learnt from the experience of previous pandemics, including HIV and COVID-19, is that local and regional capacities are fundamental to solving local and regional health challenges. Currently less than 1% of vaccines used on the African continent contain any local manufacture, according to the Africa Centre for Disease Control and Prevention. Aspen believes that this agreement assists them to achieve their commitment to expand sustainable and durable vaccine manufacturing on the continent to reduce Africa's global vaccine dependency.

FIP 2022

The International Pharmaceutical Federation's (FIP) 2022 World Congress of Pharmacy and Pharmaceutical Sciences took place from 18 to 21 September 2022 in Seville, Spain under the theme Pharmacy united in the recovery of healthcare. The co-host of this congress was the General Pharmaceutical Council of Spain.

Prior to the congress, the FIP Council met on Saturday 17, Sunday morning 18 and Thursday morning 22 September 2023. During the election of the three new FIP Vice-presidents, South Africa supported the election of Dr Prosper Haig from Cameroon, as it is important to have Africa represented on the FIP Bureau. Congratulations to Prosper!

During the FIP Council meeting, three new Statement of Policy documents were presented for adoption by the Council. For each of these three documents, a PSSA member had volunteered to participate in the working group that had developed the documents.

This was a great opportunity to share expertise from a South African perspective, but also to learn from global colleagues and

implement these new learnings locally. Jameel Kariem (PSSA CWP branch) contributed to the FIP Statement of Policy on the role of pharmacy professionals on point-of-care testing. Dr Mariet Eksteen (PSSA National Office) participated in the FIP Statement of Policy on Continuing Professional Development, while Nicole Keuler (PSSA CWP branch) was nominated to the committee who worked on the FIP Statement of Policy on Quality Assurance of pharmacy and pharmaceutical sciences education. Dr Sham Moodley (ICPA Board of Directors) participated in the FIP Statement on Access to Medicines which will be completed in 2023. Prof Yahya Choonara (University of the Witwatersrand) was appointed by the FIP Bureau to serve on the Nanjing Statement of Policy committee to review these statements during 2023.

This year, Prof. Choonara received the 2022 FIP Distinguished Pharmaceutical Science award for outstanding contributions made to pharmaceutical sciences. Andy Gray (University of KwaZulu-Natal) was also appointed as a director to the FIP Foundation. Dr Moodley was elected as executive committee member to the Community Pharmacy Section (CPS) of FIP for a 4-year term. Rendani Tshilambwana, a postgraduate student from Sefako Makgatho Health Sciences University, was the winner of the FIP Health and Medicines Information Section poster competition. Prof. Varsha Bangalee (University of KwaZulu-Natal) was recognised in absentia as FIP Champion.

At the congress, the FIP Global competency framework for educators and trainers in pharmacy (FIP-GCFE) was launched. Dr Eksteen, as global lead for the Development Goal 7 on integrated pharmacy services, co-authored this publication.

South African delegates were also involved in a number of academic sessions during the congress by chairing sessions, participating in panel discussions or presenting posters.

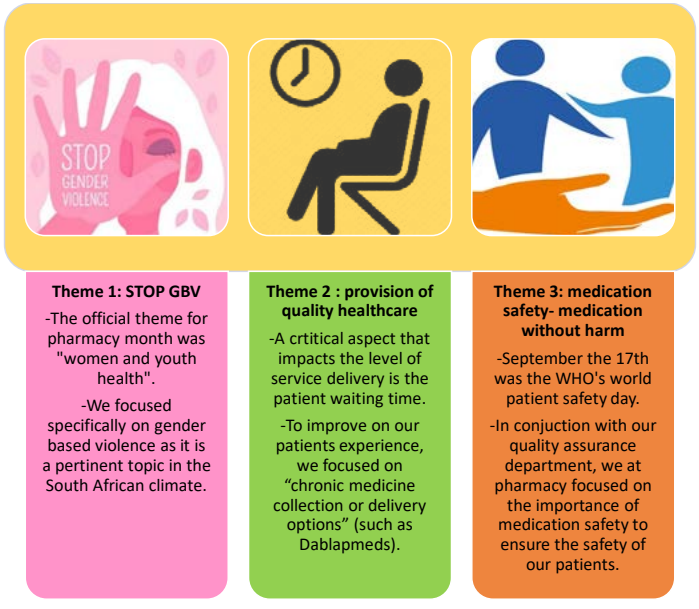
An important event is that the 82nd FIP World Congress of Pharmacy and Pharmaceutical Sciences will be hosted in Cape Town. The PSSA, as member organisation of FIP, will be the co-host of this event at the Cape Town International Convention Centre (CTICC) from 1 to 5 September 2024.

We hope to see you there!

Pharmacy month campaign: Edenvale Regional Hospital

Edenvale Regional Hospital Pharmacy initiated a week-long campaign during Pharmacy Month in order to put the spotlight on the pharmacy profession and show our patients and staff our role in quality healthcare provision. We selected three themes that are relevant to the current healthcare climate in South Africa.

The themes and reasons behind the chosen themes are illustrated in the figure below.



We implemented the following initiatives to create awareness:

- For the opening of our campaign, all staff were dressed in pink to show our support against gender based violence (GBV). We also had a special opening/welcome planned for our patients to create awareness and to generate excitement for the week ahead. The opening involved a short skit showing an ill 'patient' who feels better after receiving medication and care from the pharmacy. The skit ended with a dance routine performed by pharmacy staff and members of the hospital management team. The routine was thoroughly enjoyed by the patients and some of them even joined in on the dancing. The hospital CEO also attended the opening day and spoke to the patients about the importance of raising awareness and reporting GBV.
- Our community service pharmacist and pharmacist intern conducted daily 10-minute presentations to our patients on the topics of *CCMDD (now known as Dablapmeds)* and *Medication Safety*. They also created posters and pamphlets to serve as visual aids to support their presentation.
- An information table was set up daily and two staff members were present at the table to assist patients with any advice or guidance they might need, particularly on registering for Dablapmeds and medication-safety-related questions.
- Staff promoted awareness of GBV by providing patients with screening questionnaires and pamphlets.
- We approached various companies to supply information

leaflets/paraphernalia for patients. We also received private sponsors from people in the community who are eager to pay back to the community by showing some goodwill. These items included water, fruit and snacks.

- Edenvale Pharmacy was showcased on Alex FM. The pharmacy manager, Ms Rudzani Negondeni, was interviewed on air and spoke about the importance of raising awareness of GBV and the role of the pharmacy profession in the fight against GBV.
- We also organised training for hospital staff from various companies. The focus was on medication safety. This tied in with the WHO global patient safety day (which takes place annually on 17 September) as initiated by our QA department.
- We also organised training for pharmacy staff from our suppliers.
- These sessions were beneficial in continuing our professional development.
- Lastly, just for the spirit of pharmacy month, we also had a dress code for the remainder of the week. Each day we wore a different colour to show our unity as a team as well as support for our various causes.
- The campaign was a great success overall and it was met with great enthusiasm from staff and patients alike.

Figure 1: The decorated information table where patients could receive advice and sponsored items

Figure 2: The waiting area and dispensing windows were brightly decorated

Figure 3: Pharmacy staff and hospital management preparing for the opening welcome dance. We also had goodie bags, water and snacks for the patients, thanks to generous donations from the community as well as pharmaceutical companies

Figure 4: Pharmacy staff dressed in pink to show support for the fight against GBV

The PSSA/Alpha Pharm distance learning programme 2022

The PSSA/Alpha Pharm distance learning programme continues to offer pharmacists useful, practical, up-to-date information that enables them to provide optimal pharmaceutical care to their patients.

Module 5, 2022 – Common ear problems

The role of the pharmacist lies in identifying and assisting patients with ear disorders which can be managed in the pharmacy setting and those who require referral to the doctor.

Disorders of the outer ear include infections such as otitis externa, injuries to the ear and blockages caused by earwax. Middle ear disorders include perforation of the eardrum, barotrauma caused by unequal air pressure on the two sides of the eardrum, and infections such as otitis media. Inner ear disorders may present with symptoms such as hearing loss, vertigo, tinnitus, and congestion. Ear infections are the most common ear problems seen in infants and children, while blockages caused by accumulated earwax are more likely to happen in older people.

Although some common ear problems may be treated in the pharmacy with medicines available over-the-counter (OTC), it is not always possible to determine the underlying cause of the ear disorder without examining the inside of the ear. Unless the pharmacist is trained in clinical examination of the ear, diagnosis of an ear disorder should be made by a doctor, who can examine the ear.

The pharmacist is in the key position to educate patients about the more common ear disorders, their risk and protective factors and how they are usually treated.

The pharmacist is pivotal in ensuring that patients using medications for their ear problems use these medications safely and effectively.

For more information about this programme, contact Gill or Glynis at Insight Medicine Information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.

The PSSA/Alpha Pharm clinical education programme 2022 for pharmacy staff

The PSSA/Alpha Pharm pharmacy staff clinical education programme continues to offer front-shop assistants or pharmacist's assistants up-to-date information that enables them to provide optimal pharmaceutical care to their patients. All pharmacy staff need to be familiar with the use of unscheduled medicines and should be reminded of when it is necessary to refer the patient to the pharmacist.

Module 5, 2022 – Common ear problems

The front shop staff in the pharmacy can play a valuable supportive role in the management of common ear disorders.

Common ear problems include blockages caused by earwax and infections of the outer and middle ear. Infections are the most common ear problems seen in infants and children, while blockages caused by accumulated earwax are more likely to happen in older people. While minor ear problems such as accumulated earwax and swimmer's ear can be effectively treated in the pharmacy using simple over-the-counter medicines, the front shop member of staff needs to be on the alert for signs and symptoms that suggest a more serious ear problem that needs to be referred to the doctor.

This module discusses common ear problems seen in the pharmacy and provides guidance on the appropriate treatment of minor ear problems, as well as the recommended pointers for referral to the pharmacist or doctor.

If you would like to participate in the PSSA/Alpha Pharm pharmacy staff clinical education programme, please contact Gill or Glynis for further information on 011 706 6939 or email: cpdalphapharm@insightmed.co.za.

Recap of the PSSA conference and PIP call

PSSA Conference 2022

The YPG had the wonderful opportunity to attend the PSSA conference from 1 to 3 September at the Indaba Conference Hotel in Fourways, Johannesburg. This was both an educational and invigorating experience that provided a much needed boost of passion and desire to contribute to the profession. Each presentation provided invaluable professional information from updates to pharmacist's assistant training programmes and new specialty qualifications in pharmacy, to vaccines, the National Health Insurance, and digitalisation in pharmacy. The YPG contributed to the conference by designing the logo, editing the conference programme, and encouraging everyone to participate in a bingo game with the aim of increasing interaction amongst the delegates. The cherry on top was the YPG evening which was a light-hearted night full of entertainment.

Left to right: Alexander Wehmeyer, Nelson Mabusela, Ntombizodwa Luwaca, Roslita da Silva, Azraa Bassa, Brent Sin Hidge

"This was the first time I have attended the PSSA conference and it was a valuable experience. Each session provided valuable knowledge and information and I feel a step ahead regarding what is going on in the pharmacy profession." – Roslita da Silva (first-time attendee of a PSSA conference)

Inspirational golden nuggets from the conference

"This is no time to stop evolving, adjusting, and growing"
– Andy Gray

"Local challenges can be solved by local capabilities and capacities"
– Stavros Nicolaou

"By virtue of being a pharmacist, we are community leaders already"
– Hilton Stevens

"We are not here to have feathers and fly high, we are here to serve the profession"
– Johannes Ravele

"Leadership does not have anything to do with age, but with exposure and passion for the profession"
– Rhulani Maluleke

Feel free to reach out to us at
ypg@pssa.org.za

Facebook:
Young Pharmacists' Group of PSSA

Young pharmacists – connected, engaged, empowered and inspired!

Professional Innovation Project (PIP) 2023 Call

The PIP 2023 submission cycle is now open and we would like to invite you to apply. The goal of the PIP is to promote innovation in the profession of pharmacy and pharmaceutical sciences through supporting creative projects by young pharmacists (pharmacy practitioners and pharmaceutical sciences), which directly or indirectly benefit or improve health and demonstrate the value added by pharmacy to health. To find out more about this project and access the application forms visit the YPG's page on the PSSA website (https://www.pssa.org.za/young-pharmacists-group.html).

An addition to the YPG social media footprint

The YPG launched an Instagram page on 10 September in an attempt to cater to PSSA YPG members who may not have access to Facebook. We are happy to announce the success of this page which gained over 50 followers within the first week. We encourage you to follow the page for a video recap of the conference and interact with our health day campaigns!

Drugs used in South Africa in the management of nausea and vomiting in adults

N Schoeman

Clinical Pharmacist, Zuid-Afrikaans Hospital, South Africa

Corresponding author, email: nicolene@zah.co.za

Abstract

This article mainly summarises the available drugs approved in South Africa for preventing and treating nausea and vomiting. The mechanisms of action, indications, dosing and side effects are discussed. A quick overview of the difference between nausea and vomiting is provided, along with the pathophysiology and the approach to the management thereof. Lastly, mention is made regarding drugs used in other countries to manage nausea and vomiting.

Keywords: nausea and vomiting, emesis, antiemetics, antihistamines, dopamine antagonists, serotonin antagonists, neurokinin antagonists

S Afr Pharm J 2022;89(6):15-18

Introduction

Nausea, the distressing sensation of being about to vomit, can occur alone or in combination with vomiting, the forceful expulsion of gastric contents through the mouth, as well as indigestion and other gastrointestinal symptoms. Nausea can occur without vomiting and vomiting without nausea, although less common. Nausea is often more troublesome and incapacitating than vomiting.[1]

A variety of disorders can produce nausea with or without vomiting from medications and toxins, infections, disorders of the gut and peritoneum to CNS-, endocrinologic-, metabolic- and miscellaneous causes like postoperative nausea and vomiting (PONV).[2]

Pathophysiology

The normal functioning of the upper gastrointestinal tract (GIT) involves the gut and the central nervous system (CNS). The motor function of the gut is controlled at three main levels: the parasympathetic and sympathetic nervous systems, enteric brain neurons, and smooth muscle cells.[1]

When the gastrointestinal system senses a threat, a message is sent to the peripheral receptors, conveying the message to the central receptors in the vomiting centre. Consequently, the vomiting centre triggers nausea and vomiting by stimulating the GIT, abdominal muscles, and the diaphragm.[2]

Antiemetics

Antiemetics are medications used to treat nausea and vomiting. The term antiemetics means 'against emesis', otherwise known as vomiting. Antiemetics work on the neural pathways involved in vomiting by blocking specific receptors that respond to neurotransmitter molecules.[2]

Five principal neurotransmitter receptors facilitate vomiting: M1 (muscarinic), D2 (dopamine), H1 (histamine), 5-hydroxytryptamine (HT)-3 (serotonin) and NK1 (Neurokinin 1) through substance P.[1]

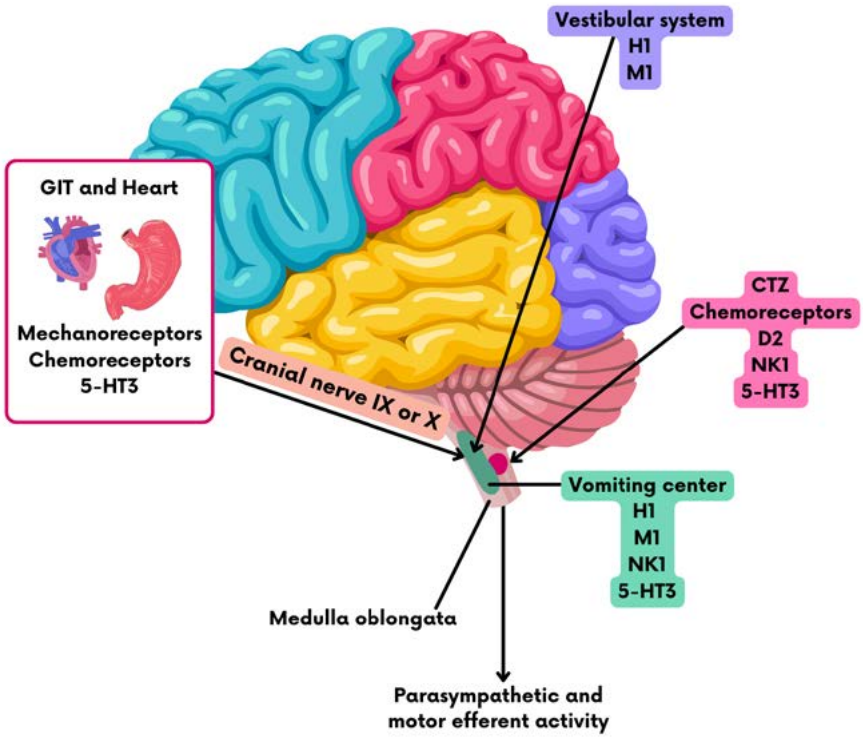


Figure 1: Receptor sites[3]
GIT – gastrointestinal tract

Table I: Classification, drugs, and site of action of the antiemetic drugs registered in SA[4]

Class	Drugs	Site of action
Antihistamines	promethazine, cyclizine, buclizine, cinnarizine, betahistine	Emetic centre, cerebral cortex
Dopamine antagonists: phenothiazines	prochlorperazine, promethazine	CTZ
Dopamine antagonists: butyrophenones	droperidol	CTZ
Dopamine antagonists: benzamides	metoclopramide*, domperidone	CTZ, peripheral*
Serotonin antagonists	granisetron, ondansetron, palonosetron	Emetic centre, peripheral
Neurokinin antagonists	aprepitant, fosaprepitant	Cerebral cortex, peripheral

CTZ – chemoreceptor trigger zone

M1, D2, 5-HT3, and NK1 receptors are found in the area postrema (AP), also known as the chemoreceptor trigger zone (CTZ). Other central and peripheral sites play a role, including H1 receptors in the vestibular nucleus and 5-HT3 receptors on the vagus nerve. Figure 1 shows the receptor sites[3]

Approach to management

In patients presenting with nausea and vomiting, the following should be considered:[3]

- The cause, whether it's acute nausea and vomiting or chronic (at least one month in duration).
- The consequences of nausea and vomiting (e.g., fluid depletion, hypokalaemia, and metabolic alkalosis) should be identified and corrected.
- Therapy should be individualised based on cause, severity, the preferred route of administration, safety, and costs.

Treatment of nausea and vomiting

South Africa (SA) has several registered drugs for preventing and treating nausea and vomiting, as shown in Table I. Antiemetics are classified according to the main neurotransmitter receptor that they act on, which is involved in the physiology of nausea and vomiting.[4]

Antiemetic drugs

Antihistamines

H1 antagonists are often used to treat and prevent nausea and vomiting induced by vertigo or motion sickness. Sedation is a common side effect of this class.[1]

Available antihistamine drugs indicated for nausea and vomiting in SA include promethazine, cyclizine, buclizine, cinnarizine and betahistine.

Promethazine has both antihistamine and dopamine-antagonising properties. Betahistine has antagonising effects on both H1 and H3 receptors.

Dopamine antagonists

Dopamine antagonists are amongst the most used antiemetics, indicated for PONV and motion sickness.[2]

There are three classes of dopamine receptor antagonists used in nausea or vomiting: phenothiazines, butyrophenones and benzamides. Figure 2 lists the classes of dopamine antagonists with the available drugs in SA.[1]

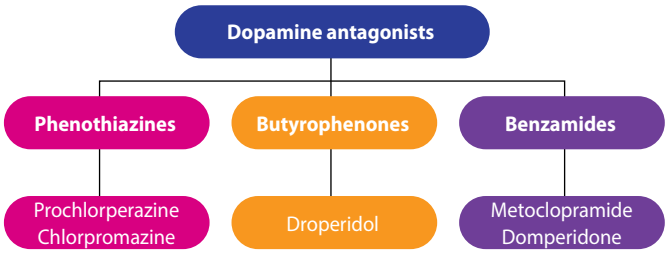


Figure 2: Dopamine antagonists and available drugs in SA[1]

Phenothiazines

The phenothiazines predominantly block D2-dopamine receptors in the CTZ and M1 and H1 receptors, demonstrating considerable activity in the prevention of chemotherapy-induced emesis (CIE).[1]

Available drugs include prochlorperazine and chlorpromazine.

Extrapyramidal reactions such as dystonia, and with prolonged use, tardive dyskinesia, is a common side effect of this class.[1]

Prochlorperazine

Prochlorperazine is the most used antiemetic in this class. It is moderately effective to alleviate acute nausea and vomiting from gastrointestinal disorders (e.g., acute gastroenteritis) and in patients receiving mild to moderate but not highly emetogenic chemotherapy.[1]

Chlorpromazine is used less often than prochlorperazine.

Butyrophenones

Butyrophenones, when used alone, have an antiemetic effect, although they are typically used as major tranquillizers to potentiate the action of opioids. They are primarily used as a pre-medication but are also effective for PONV.[1]

The only drug available in SA is droperidol.

The side effect profile and antiemetic efficacy are comparable to the phenothiazines. Intravenous administration of droperidol may cause QTc prolongation and Torsade's de pointes. Thus, patient monitoring is advised before and for two to three hours after administration. Additional side effects include hypotension, alpha blockade, and acute dystonia.[1]

Table II: Registered indication and dosing of antiemetics available in SA

Antiemetic drug	Indication	Dosing
Antihistamines		
Promethazine	Vertigo Motion sickness	25 mg, 12 hourly, PRN IV/IM
Cyclizine	Motion sickness	50 mg PO, 1–2 hours before departure, repeated 8 hourly PRN
Buclizine	Motion sickness chemo-/radiotherapy NV	Motion sickness 25–50 mg PO, 1–2 hours before departure Chemo-/radiotherapy NV 50 mg PO, 6–8 hourly; initiated 1–2 days before exposure to chemo/radiotherapy
Cinnarizine	Labyrinthine disorders Motion sickness	Labyrinthine (including vertigo, NV) 25–75 mg PO, 8 hourly **Max: 225 mg/24 hours** Motion sickness 50 mg PO, 1 hour before departure; repeat 25 mg, 8 hourly PRN
Betahistine	Vertigo associated with Ménière's Syndrome	Initial: 24 mg, 12 hourly, take with food Maintenance: 24–48 mg/day in divided doses **Max: 48 mg/24 hours**
Dopamine antagonists		
Phenothiazines		
Prochlorperazine	Prevention and treatment of NV Labyrinthine disorders	Prevention of NV 5–10 mg PO, 8–12 hourly Treatment of NV PO: 20 mg STAT, 10 mg 2 hours later PRN Rectal (sup): 25 mg, further doses to be given orally IM: 12.5 mg, further doses to be given orally Labyrinthine disorders Initial: 5 mg, 8 hourly PO; increase to 30 mg daily; after several weeks, decrease to 5 mg daily
Chlorpromazine	NV in terminal illness	PO: 10–25 mg, 4–6 hourly IM: 25–50 mg; may repeat 3–4 hourly until vomiting stops, then change to oral
Butyrophenones		
Droperidol	NV	Prevention and treatment of NV: surgical and diagnostic procedures IV/IM: 2.5 mg as a single dose Prevention and treatment of NV: induced by morphine derivatives during postoperative controlled analgesia IV/IM: 25 µg per 1 mg of morphine **Max: 5 mg/24 hours**
Benzamides		
Metoclopramide	NV because of postoperative, medicine-induced, uraemic conditions, malignant disease, gastrointestinal disorders, post anaesthetic vomiting, post chemo- /or radiotherapy, acute migraine-induced	IV/IM: 10 mg, 8 hourly if needed or 0.5 mg/kg/24 hours Oral: 10 mg, 8 hourly if needed **Max: 30 mg/24 hours or 0.5 mg/kg/24 hours** **Max treatment duration: 5 days**
Domperidone	NV of central or local origin Post-cytotoxic chemo-/radiotherapy NV	Oral: 10 mg, 8 hourly **Max: 30 mg/24 hours** **Max treatment duration: 1 week**
Serotonin receptor antagonists		
Ondansetron	Management of nausea and vomiting induced by cytotoxic chemo-/ and radiotherapy Prevention and treatment of PONV	Dosing differs based on indication – see reference guidelines. Typical dosing includes: 8 mg PO/IV/IM single or 12 hourly 16 mg single IV STAT dose depending on indication
Granisetron		Dosing differs based on indication – see reference guidelines. Typical dosing includes: Oral: 1 mg, 12 hourly OR 2 mg daily; IV/IM 1–3 mg (10–40 µg/kg) **Max: 9 mg/24 hours**

Palonosetron	Prevention of acute NV associated with moderate to highly emetogenic cancer chemotherapy	IV: 250 µg as a single bolus over 30 seconds, 30 minutes before chemotherapy
Neurokinin receptor antagonists		
Aprepitant	Chemotherapy-induced NV	Day 1: 125 mg PO, 1 hour before chemotherapy Day 2–3: 80 mg PO, daily in the morning
Fosaprepitant		IV: Day 1: 150 mg infused over 20–30 minutes; initiate 30 minutes before chemotherapy

PRN – pro re nata (as needed), IV – intravenous, IM – intramuscular, PO – per os (oral), NV – nausea and vomiting, PONV – postoperative nausea and vomiting

Benzamides

Available drugs include metoclopramide and domperidone.

Metoclopramide

Metoclopramide has combined antiemetic and prokinetic properties, working on central and peripheral dopamine D2 receptors at low doses, and exerting weak 5-HT3 blockade at higher doses. At standard doses, metoclopramide is a modest antiemetic. Additionally, it increases gastric emptying in patients with gastroparesis and lowers the oesophageal sphincter tone.[1]

Metoclopramide crosses the blood–brain barrier, and as such, side effects include extrapyramidal symptoms, anxiety, restlessness, and depression. Metoclopramide has a black box warning related to the risk of irreversible tardive dyskinesia with higher dosing and long-term use, especially in the elderly. Hyperprolactinaemia and QT interval prolongation may also be experienced.[1]

Domperidone

Domperidone is a D2-blocker with selective peripheral activity in the upper GIT. Domperidone does not cross the blood–brain barrier and therefore lacks the neurological side effects of metoclopramide.[1]

Serotonin receptor antagonists

The 5-HT3 receptor antagonists form the foundation of therapy in controlling acute CIE but can also be used in acute gastroenteritis or for PONV.[1]

Three 5-HT3 antagonists are currently approved in SA: ondansetron, granisetron and palonosetron.

When used at effective doses, comparative studies have failed to show a credible difference in efficacy or tolerability between ondansetron and granisetron. Palonosetron has a higher receptor binding affinity and a considerably longer half-life.[1]

5-HT3 antagonists are generally well tolerated. The most common side effects include headaches, asthenia, constipation, and dizziness. However, electrocardiogram (ECG) interval changes may be observed with ondansetron and granisetron presenting typically as small and clinically insignificant, one to two hours after administration and returning to baseline within 24 hours. Additionally, potentially fatal cardiac arrhythmias in association with QTc prolongation have been reported. As such, ECG monitoring is recommended in patients with electrolyte abnormalities, heart failure, arrhythmias, or in those using concomitant drugs that affect the QTc interval.

Neurokinin receptor antagonists

The emetogenic effects of substance P are mediated through the NK1 receptor. NK-1 antagonists are used to suppress radio- and chemotherapy-induced nausea and vomiting, as well as in the prevention of PONV.[1]

Available drugs include aprepitant and fosaprepitant.

Compared to ondansetron and granisetron, they prevent acute and delayed emesis in patients treated with highly emetogenic chemotherapy drugs. However, NK1- antagonists work best when combined with 5HT-3 antagonists and dexamethasone.

NK1 receptor antagonists are moderate inhibitors of the enzyme Cytochrome (CYP) 3A4; as such, a dose reduction may be necessary when used concurrently with other medication primarily metabolised through CYP3A4.

Other drugs used outside of SA

Drugs used in other countries in the management of nausea and vomiting include anticholinergics (scopolamine), cannabinoids, benzodiazepines (lorazepam, alprazolam), glucocorticoids (dexamethasone) and thienobenzodiazepines (olanzapine).

Table II provides a summary of the registered indication and dosing of the antiemetics available in SA.

Conclusion

Several different classes of antiemetics are available in SA. Antiemetics are classified according to the primary receptor on which they exert an effect. Five neurotransmitter receptor sites are important in the vomiting reflex: M1 – muscarinic, D2 – dopamine, H1 – histamine, 5-hydroxytryptamine (HT)-3 – serotonin and Neurokinin-1 (NK1) receptor – substance P. Nausea and vomiting should be managed based on the individual cause, predominantly involved receptor, severity, the preferred route of administration, safety, and costs.

References

1. Constantini L. Antiemetics. [Internet]. Osmosis; c2022. Available from: https://www.osmosis.org/answers/antiemetics. Accessed 19 Oct 2022.
2. Heckroth M, Luckett R, Moser C, Parajuli D, Abell T. Nausea and vomiting in 2021: a comprehensive update. J Clin Gastroenterol. 2021;55(4):279-99. https://doi.org/10.1097/mcg.0000000000001485.
3. Longstreth G, Hesketh P. Characteristics of antiemetic drugs. [Internet]. Uptodate.com; c2022. Available from: https://www.uptodate.com/contents/characteristics-of-antiemetic-drugs?topicRef=2537&source=see_link#H101749640. Accessed 19 Oct 2022.
4. Online.lexi.com. 2022. Management of chemotherapy-induced nausea and vomiting in adults. [Internet] Available from: https://online.lexi.com/lco/action/doc/retrieve/docid/multinat_f/4667418?cesid=08ms18PJOpu&searchUrl=%2Flco%2Faction%2Fsearch%3Fq%3Dnausea%2Band%2Bvomiting%2Badult%26t%3Dname%26acs%3Dtrue%26acq%3Dnau. Accessed 19 Oct 2022.

Migraine: an evidence-based approach

A Richardson

Neurologist in Private Practice, Christian Barnard Hospital, South Africa

Corresponding author, email: reception@capeneuro.com

Abstract

Migraine is a common disabling primary headache disorder. Migraine management approaches include treatment of the acute attack and, depending on severity and frequency, providing agents to prevent further episodes. This brief review outlines the salient points of migraine management for general practitioners.

Keywords: migraine, headache, prodrome, aura, prophylaxis

Republished from: *South African General Practitioner.* 2022;3(3):87-88 **S Afr Pharm J 2022;89(6):19-20**

Introduction

Headache disorders are classified by the ICHD-III[1] as primary headache disorders, which include migraine, tension-type headache, cluster headache and other trigeminal autonomic cephalalgias, as well as other primary headache disorders, and secondary headache disorders which include a new headache occurring with another lesion capable of causing it (e.g., headache attributed to intracranial tumour). Migraine is a syndrome characterised by periodic headaches with complete resolution between attacks. The frequency of attacks is variable, occurring as low as several per lifetime to as high as several per week. Headache frequency may predict progression from episodic to chronic migraine.[2]

An attack may be composed of the following sequential stages: prodrome, aura, headache and resolution. A prodrome is a vague change in mood or appetite, while an aura is a clear neurological symptom such as a visual (flickering lights, spots or lines, and/or partial loss of vision), motor (speech) or sensory (numbness and/or pins and needles) disturbance. The moderate to severe pulsating pain may be uni- or bilateral, lasting up to 72 hours. In children, migraine is a diagnosis of exclusion.[3]

Migraine is the second most prevalent neurological disorder (after tension-type headache), with a female-to-male ratio of 3:1 and an estimated one-year prevalence of approximately 15% in the general population.[4] The prevalence peaks between the ages of 35 and 39 years, and about 75% of affected persons report the onset of migraine before the age of 35 years.[4] Since the disorder tends to remit with older age, onset of migraine after the age of 50 years should arouse suspicion of a secondary headache disorder.[4]

Acute treatment

The evidence-based National Institute for Health and Care Excellence (NICE) guidelines[5] suggest that for the acute treatment of migraine, combination therapy of an oral triptan (sumatriptan, zolmitriptan, rizatriptan, naratriptan or eletriptan) with either an NSAID (e.g. naproxen or ibuprofen), or with paracetamol, should be offered, taking the person's preference, comorbidities and risk of adverse events into account. These are best taken early in the attack when absorption may be least inhibited by gastric stasis. For people in whom oral preparations for the acute treatment of migraine are ineffective or not tolerated, a non-oral preparation of metoclopramide or prochlorperazine should be considered. An antiemetic such as metoclopramide or domperidone not only relieves the nausea that accompanies many migraine attacks but also enhances the efficacy of simultaneously administered oral analgesics.[7] Adding a non-oral NSAID or triptan if these have not been tried, should also be considered. Codeine or dihydrocodeine, which are used extensively in OTC combination analgesics[6] should not be used as they provide small additional benefit in a range of painful conditions, but evidence of this does not extend to headache and it is at the expense of increased side effects. In addition, these opioids are frequently implicated in medication overuse headache.

Prophylactic management of migraine with or without aura

Identifying and avoiding trigger factors can reduce the frequency of migraine attacks by up to 50%. It is often of value to ask the patient to keep a migraine diary recording frequency, duration and severity of attacks and to use this to monitor how effective headache interventions are. Only migraine recurring four or more times per month should be treated prophylactically.[7] It is important to review the need for continuing migraine prophylaxis six months after the start of preventative treatment.

Topiramate or propranolol

Topiramate (target dose 100 mg twice a day) or propranolol (target dose 60 mg once or twice a day) are the NICE-recommended first-line agents for the prophylaxis of migraine and these agents should be offered after a full discussion of the benefits and risks of each.[5] Topiramate should be started at a low dose (25 mg a day), and the dose should be increased over a period of two to three weeks to minimise side effects which may include cognitive slowing with perceived memory deficits and word-finding difficulties.

The risk of reduced effectiveness of hormonal contraceptives with topiramate, and the risk of foetal malformations with its use **must** be explained to your female patients. The importance of effective contraception (e.g. medroxyprogesterone acetate depot injection, an intrauterine method or combined hormonal contraception with a barrier method) for women and girls of childbearing potential who are taking topiramate should be emphasised. People with depression and migraine could be at an increased risk of worsening depression/anxiety with topiramate – in these cases, I find it beneficial to either start a concomitant antidepressant agent (usually an SSRI will suffice), or to use an alternative like valproate (300–1 000 mg BD)/pregabalin (25–75 mg BD), with the same safety/side effect information applying as above. Valproate may be limited by its somnolence, weight gain, hair loss, and possible hepatotoxicity and thrombocytopenia.

Amitriptyline

Amitriptyline is also an option for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events. I do find this less effective than the above, but it is a good starting point, and often addresses the tension-type component that accompanies migraines. Amitriptyline 10–150 mg daily, at or one to two hours before bedtime, is first-line when migraine co-exists with troublesome tension-type headache, another chronic pain condition, disturbed sleep or depression.[8] With the exception of the depressed patient, it is wise to explain the choice of this drug to patients who do not consider themselves depressed or they may reject it. Commonly reported adverse events include dry mouth, sedation, dizziness and nausea. These are most apparent in the first couple of weeks and usually settle with continued use.

Gabapentin should **not** be offered for the prophylactic treatment of migraine.

Migraine prophylaxis with botulinum toxin[9]

If topiramate, valproate, trepiline, pregabalin and propranolol are unsuitable or ineffective, consider referral to a specialist for Botox (155 units subcutaneously), but this is often limited by cost.

Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine (defined as headaches on at least 15 days per month of which at least eight days are with migraine) that has not responded to at least three prior pharmacological prophylaxis therapies and whose condition is appropriately managed for medication overuse.

CGRP monoclonal antibodies

Monoclonal antibodies to the calcitonin gene-related peptide (CGRP) pathway or its receptor may reduce disability even on non-headache days,[1] and may be useful treatment options in the future.[10]

Conclusion

Migraine management can often be tricky, particularly as it often co-exists with other pathologies, and it is useful to approach the patient not only from a medication aspect, but to also discuss the non-medical supporting therapies, such as triggers, physiotherapy, keeping a headache diary, management of stress and anxiety and the like. With the advent of the CGRP monoclonal antibodies, due to be available in SA in the near future, it is likely that migraine management will see a shift from the current therapies to these more targeted therapies.

References

1. Arnold M. Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd ed. Cephalalgia. 2018;38:1-211. https://doi.org/10.1177/0333102417738202.
2. Xu J, Kong F, Buse DC. Predictors of episodic migraine transformation to chronic migraine: a systematic review and meta-analysis of observational cohort studies. Cephalalgia. 2020;40(5):503-16. https://doi.org/10.1177/0333102419883355.
3. GP notebook. Migraine. Available from: https://gpnotebook.com/simplepage.cfm?ID=-1670709238. Accessed Mar 2022.
4. Ashina M. Migraine. N Engl J Med. 2020;383:1866-76. https://doi.org/10.1056/NEJMra1915327.
5. NICE. Headaches in over 12s: diagnosis and management. Clinical guideline [CG150] Published date 2012; updated December 2021. Available from: https://www.nice.org.uk/guidance/cg150/chapter/Recommendations. Accessed Mar 2022.
6. British Association for Study of Headache guidelines, 2004. Available from: https://www.bash.org.uk/page/1/?s=headache+guidelines. Accessed Mar 2022.
7. Managing migraine. Drug Ther Bull. 1998;36(6):41-44. https://doi.org/10.1136/dtb.1998.36641.
8. Ahmed F. Headache disorders: differentiating and managing the common subtypes. Br J Pain. 2012;6(3):124-32. https://doi.org/10.1177/2049463712459691.
9. Becker D, Amirlak B. Beyond beauty: Onobotulinumtoxin A (BOTOX®) and the management of migraine headaches. Anesth Pain Med. 2012;2(1):5-11. https://doi.org/10.5812/aapm.6286.
10. Tso AR, Goadsby PJ. Anti-CGRP monoclonal antibodies: the next era of migraine prevention? Curr Treat Options Neurology. 2017;19(8):27. https://doi.org/10.1007/s11940-017-0463-4.

OTC management of soft-tissue sports injuries

N Schoeman

Clinical Pharmacist, Zuid-Afrikaans Hospital, South Africa

Corresponding author, email: nicolene@zah.co.za

Abstract

The location and accessibility of community pharmacies put pharmacists in the ideal position to assist patients with the appropriate management of soft-tissue sports injuries. Pharmacists should, therefore, be able to provide appropriate advice and recommendations. Research has indicated that effective early management can reduce pain, promote rapid healing, and shorten rehabilitation. Advances in non-pharmacological measures include a new acronym, PEACE and LOVE, encompassing healing from immediate care to subsequent management. Short-term pharmacological treatment mainly consists of nonsteroidal anti-inflammatory drugs (NSAIDs) and should only be initiated after the first 24–48 hours of an acute injury.

Keywords: soft-tissue injuries, acute musculoskeletal injuries, muscle pain, sprains, strains, NSAIDs, analgesics, opioids

S Afr Pharm J 2022;89(6):21-24

The role of pharmacists in the management of soft-tissue sports injuries

The location and accessibility of community pharmacies mean patients are likely to present at the pharmacy with soft-tissue-related sports injuries. Pharmacists thus play a key role in treating, preventing, and referring typical soft-tissue sports injuries.[1] Therefore, pharmacists should be able to determine whether the injury is mild or self-limiting, whether it can be managed with appropriate self-care and advice, over-the-counter (OTC) medicine or whether the patient needs a referral.[2]

In addition, pharmacists can be a valuable resource for patients and caregivers seeking advice regarding OTC analgesics and nonpharmacologic measures for managing sports injuries.[3] Research has shown that patients often take OTC pain medication inappropriately due to their perceived safety, and as such, pharmacists should advocate for the responsible and safe use of OTC pain medicine due to the associated adverse effects, the potential for opioid-dependency and drug–drug interactions.[4,5]

Managing soft-tissue injuries is about more than short-term damage control; favourable long-term outcomes should be the goal. Better education on soft-tissue injuries helps to avoid overtreatment, reducing the likelihood of unnecessary injections or surgery. Additionally, realistic, optimistic expectations about recovery times instead of chasing a quick fix are associated with better outcomes.[5]

Assessment and management of injury in the pharmacy

Effective early management can reduce pain, promote rapid healing, and shorten rehabilitation and as such, taking a thorough history from the patient is vital.[2]

Points to consider when taking a history from the patient[2]

- Is this an acute or chronic injury?
- If acute – when did this injury happen?
- Has the injury been treated?
- If yes – what was the treatment?
- Was the patient able to continue with their activity?
- What was the intensity of the activity leading up to sustaining the injury?
- Has this or any other injury occurred before?
- Other medical history, including medication.

The following patients should be referred[2]

- Patients presenting with deformity, inability to use or bear weight on the limb or severe pain could indicate a fracture or dislocation.
- Patients with injuries to the head, cervical spine, or the thoracic or abdominal organs.
- Patients with suspected concussion following a blow to the head, face, and neck who present with changes in behaviour, vomiting, dizziness, headache, double vision or excessive drowsiness.
- Recurrent injuries.

Non-pharmacological management

Soft-tissue injuries simply need PEACE and LOVE[5]

Over the years, acronyms guiding the management of soft-tissue injuries have evolved from ICE to RICE to PRICE and POLICE. Unfortunately, these acronyms focus on acute management, ignoring subacute and chronic stages of tissue healing. A new acronym PEACE and LOVE embraces the treatment continuum from immediate care (PEACE) to successive management (LOVE). Figure 1 describes this acronym.

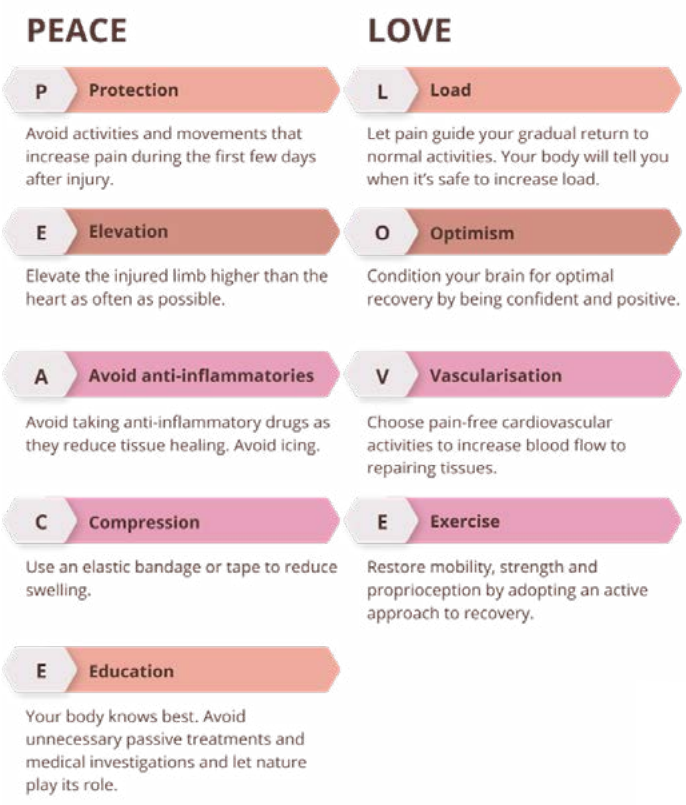


Figure 1: PEACE and LOVE acronym explained[5]

PEACE should guide the management approach to a soft-tissue injury immediately after the injury. As such, movement and load should be restricted for the first 1–3 days to reduce bleeding, limit swelling of injured fibres and decrease the risk of exacerbating the injury. Whereafter rest should be restricted as extended rest can compromise tissue strength and quality.[5]

It is crucial to understand that various phases of inflammation are involved in the repair of damaged soft tissue. Thus, inhibiting inflammation using medications may negatively affect long-term tissue outcomes. The standard of care for soft-tissue injuries should thus not include anti-inflammatories during the acute phase of the injury.[5]

After the first three days, soft-tissue injuries need LOVE, as outlined in figure 1.

Cardiovascular activity forms the cornerstone in managing musculoskeletal injuries; therefore, pain-free aerobic exercise should be started a few days after injury to boost motivation and increase blood flow to the injured soft tissue. Optimal loading without aggravating pain promotes repair, remodelling and builds tissue tolerance and the capacity of tendons, muscles and ligaments, reducing the need for pain medication.[5]

Soft-tissue injuries

The most common soft tissues injured are muscles, tendons, and ligaments.[6]

Soft-tissue injuries are divided into two categories: acute injuries and overuse injuries:[6]

Acute injuries occur due to sudden trauma, such as a fall, twist, or blow to the body. Examples include sprains, strains, and contusions.

Overuse injuries occur progressively over time due to repetitive trauma. Tendinitis and bursitis are common soft-tissue overuse injuries.

Symptoms of soft-tissue injuries may include pain, swelling, inflammation, muscle spasm, muscle weakness and bruising.[6]

Common acute soft-tissue injuries

Sprains

A sprain is a stretch and/or tear of a ligament. Ligaments stabilise and support the body's joints. The areas of the body that are most susceptible to sprains are the ankles, knees, and wrists. Sprains are classified by severity (Table I).[6]

Table I: Sprain classification

Grade	Severity	Presentation
1	**Mild**	Slight stretching and some damage to the fibres of the ligament
2	**Moderate**	Partial tearing of the ligament; there is abnormal laxity in the joint when it moves in certain ways
3	**Severe**	Complete tear of the ligament; this may cause considerable instability

While the severity varies, pain, bruising, and inflammation are common in all three categories of sprains. Mild sprains treatment begins with PEACE and LOVE. Moderate sprains may require a period of bracing. Severe sprains may require surgery.

Strains

A strain is an injury to a muscle and/or tendon. Tendons are fibrous cords of tissue that attach muscles to bone. Strains often occur in the back or leg. Like a sprain, a strain may be a simple stretch of a muscle or tendon, or it may involve a partial or complete tear of the muscle and tendon. The recommended treatment for a strain is the same as for a sprain.[6]

Contusions/bruises

Contusions occur due to a direct blow to the body, crushing underlying muscle fibres and connective tissue without breaking the skin. Discolouration of the skin is caused by blood pooling around the injury. Most contusions are mild and respond well to PEACE and LOVE. If symptoms persist, the patient should be referred to prevent permanent damage to the soft tissues.[6]

Common soft tissue overuse injuries

Tendinitis

Tendinitis is the inflammation or irritation of a tendon or the covering of a tendon that occurs due to repeated small stresses.[6]

Bursitis

Bursae are small, jelly-like sacs containing a small amount of fluid to help cushion and reduce friction. They are positioned

throughout the body between bone and soft tissues, around the shoulder, elbow, hip, knee, and heel.[6]

Bursitis is inflammation of a bursa. Repeated small stresses and overuse can cause the bursa to swell.[6]

OTC management of soft-tissue sports injuries in adults

The latest American College of Physicians (ACP) and the American Academy of Family Physicians (AAFP) guidelines for the pharmacological management of acute pain related to soft-tissue injuries recommend the following:[7]

- Topical nonsteroidal anti-inflammatory drugs (NSAIDs), with or without menthol gel, should be used as first-line therapy.
- Oral NSAIDs and paracetamol may be considered as options for pharmacologic treatment.
- Opioids should not be used as first-line treatments. The severity of the injury, patient intolerance of other treatments, and potential harms should be considered before starting treatment with opioids.

Nonsteroidal anti-inflammatory drugs

PEACE and LOVE should be recommended as first-line treatment in the management of soft-tissue injuries. However, patients may also require pain relief and whilst anti-inflammatories show benefits in the reduction of pain and function, there is a growing body of evidence indicating that the use of anti-inflammatories in the acute inflammatory phase (during the first 24–48 hours post-injury) may be detrimental. As such, it should not be included in the standard management of soft-tissue injuries during the first 48 hours.[5]

Should inflammation be a component of the injury and no contraindications are present, evidence does support the short-term use of NSAIDs for the management of soft-tissue injuries, to provide pain relief, decrease heat around the affected area, decrease swelling, improve mobility, and allow for earlier continuation of normal activity.[8]

The mechanism of action of NSAIDs involves inhibiting the production of pain-mediating prostaglandins. In general, NSAIDs provide a comparable degree of pain and inflammatory relief, and as such, the decision should be based on the patient's personal preference and experience, safety profiles, cost, and convenience.[9]

OTC NSAIDs include
- Aspirin
- Ibuprofen
- Diclofenac
- Mefenamic acid
- Piroxicam
- Naproxen

Table II provides an overview of the active ingredients, their indication, dosing, and side effects.

Topical nonsteroidal anti-inflammatory drugs

Patients are unlikely to gain any added benefit by using topical NSAIDs as an adjunct to oral NSAID therapy. Topical NSAIDs as sole therapy may be helpful if the patient cannot tolerate oral NSAIDs.[9]

Topical NSAIDs can be applied directly to the affected area. This causes therapeutically significant concentrations in the underlying inflamed soft tissues, whilst limiting associated systemic side effects (e.g., gastrointestinal bleeding and renal impairment).[9]

Local side effects may include skin (e.g., dermatitis, pruritis or erythema) and photosensitivity reactions, which usually resolve once treatment is stopped.[9]

Available OTC topical NSAIDs include:
- Ibuprofen
- Diclofenac
- Ketoprofen
- Indomethacin

Paracetamol

Due to its excellent safety profile and lack of any significant side effects, paracetamol is the drug of choice in pain management. However, it does not offer anti-inflammatory effects.

The precise mechanism of action for its analgesic properties is not fully understood, but it appears that paracetamol acts predominantly by inhibiting prostaglandin synthesis in the central nervous system (CNS) and, to a lesser extent, through a peripheral action by blocking pain impulse generation. See Table II for dosing and side effects.[9]

Opioid analgesics

Patients reporting inadequate pain relief from paracetamol and NSAIDs may benefit from supplemental short-term opioid therapy. Caution is advised in patients with a history of drug abuse and seizures and those on CNS depressing agents.[9]

The only available OTC opioid in South Africa is codeine. Codeine is a centrally-acting weak analgesic. It exerts its effect through mu-opioid receptors, resembling morphine in its pharmacodynamic actions, although much weaker in its effects.[9]

Opioid use is limited by its side effects and risk for dependency, which may occur even at OTC doses, particularly with prolonged use.[9]

Muscle relaxants

In cases where soft-tissue pain does not subside with the use of the abovementioned NSAIDs and/or analgesics, muscle relaxants may also reduce pain and discomfort.[9]

Muscle relaxants work by altering central nerve conduction.

OTC available preparations include orphenadrine and metho-carbamol.

Table II: OTC medicine used in the management of soft-tissue sports injuries[9]

Active ingredient	Indication	Dosing	Side effects
NSAIDs			
Aspirin	Mild to moderate pain Fever Inflammation	300–600 mg, 3–4 hourly as required **Max: 3.6 g/24 hours**	Gastric erosion and bleeding, peptic ulceration Hypersensitivity reactions: skin rashes, pruritus, and angioedema Renal toxicity
Ibuprofen		1 200–1 800 mg daily, in divided doses Maintenance range: 600–1 800 mg daily, in divided doses **Max: 2 400 mg/24 hours**	
Diclofenac		Oral (tab, caps, sac): Initial: 25–100 mg, as a **single dose** Maintenance: 25–50 mg, 8 hourly Oral (dsp): 100–150 mg, 8–12 hourly **Max: 150 mg/24 hours**	
Mefenamic acid		500 mg, 8 hourly **Max: 1 500 mg/24 hours**	
Piroxicam		Initial: 20 mg daily Maintenance: 10–20 mg daily **Max: 20 mg/24 hours**	
Naproxen		Initial: 500 mg, then 250 mg, 6–8 hourly **Max: 1 250 mg/24 hours**	
Analgesic			
Paracetamol	Mild to moderate pain Fever	500–1 000 mg, 4–6 hourly **Max: 4 000 mg/24 hours**	Hypersensitivity skin reactions Neutropenia Thrombocytopaenia Nephrotoxicity Hepatotoxicity
Muscle relaxants			
Orphenadrine Citrate	Muscle spasm associated with acute musculoskeletal conditions	100 mg, 8–12 hourly	CNS depression-associated side effects (drowsiness, confusion, memory disturbances) Urinary retention, Hypersensitivity reactions
Methocarbamol		Initial: 1 500 mg, 6 hourly for 2–3 days Maintenance: 750–1 000 mg, 6 hourly **Max: 8 g/24 hours**	CNS depression-associated side effects (drowsiness, confusion, memory disturbances) Hypersensitivity reactions Metallic taste

Orphenadrine is an anticholinergic/antihistaminic drug with good CNS penetration, making it an ideal drug to treat pain of varying aetiologies.

Methocarbamol is a centrally-acting muscle relaxant of which the precise mechanism of action is unknown.

Conclusion

Pharmacists play an essential role in determining whether an injury is mild or self-limiting, and subsequently educating on the importance of applying PEACE and LOVE, advising on OTC medicine, and referring patients if necessary. Soft-tissue injuries should be managed with the goal of favourable long-term outcomes, and as such, early management should be implemented to reduce pain, promote healing, and shorten rehabilitation. Emphasis should be placed on the fact that standard management of soft-tissue injuries during the first 48 hours should not include anti-inflammatories. Instead, non-pharmacological measures, as described by PEACE and LOVE, should be implemented. OTC pharmacological management of soft-tissue injuries may include NSAIDs, paracetamol, opioids or muscle relaxants and should be based on the patient's injury, history of medication use, personal preference and experience, safety profiles, cost, and convenience.

References

1. Maffulli N, Longo UG, Gougoulias N Caine D, Denaro V. Sport injuries: a review of outcomes. Br Med Bull. 2011;94:47-80. https://doi.org/10.1093/bmb/ldq026.
2. Thomas T, Mottram D, Waldock C. Advising patients on prevention and management of sporting injuries in the pharmacy. The Pharmaceutical Journal. 2016;297(7892);297. https://doi.org/10.1211/PJ.2016.20201530.
3. Hooper AD, Cooper JM, Schneider J, Kairuz T. Current and potential roles in sports pharmacy: a systematic review. Pharmacy (Basel). 2019;7(1):29. https://doi.org/10.3390/pharmacy7010029.
4. Terrie YC. (2021) Managing sports injuries in adolescents. Pharmacy Times. 2017;83(3). Available from: https://www.pharmacytimes.com/view/managing-sports-injuries-in-adolescents. Accessed 25 Oct 2022.
5. Dubois B, Esculier J-F. Soft-tissue injuries simply need PEACE and LOVE. Br J Sports Med. 2020;54(2):72-73. https://doi.org/10.1136/bjsports-2019-101253.
6. Mulcahey MK. Sprains, strains and other soft-tissue injuries. [Internet]. OrthoInfo; c1995-2021. Available from: https://orthoinfo.aaos.org/en/diseases--conditions/sprains-strains-and-other-soft-tissue-injuries/. Accessed 25 Oct 2022.
7. American Academy of Family Physicians (AAFP). Musculoskeletal (MSK) Clinical Recommendations & Guidelines. [Internet]. American Academy of Family Physicians; c2022. Available from: https://www.aafp.org/family-physician/patient-care/clinical-recommendations/recommendations-by-topic/musculoskeletal-clinical-recommendations-guidelines.html. Accessed 25 Oct 2022.
8. Levy DB. Knee soft tissue injury (ACL, LCL, MCL, PCL) management in the ED medication. [Internet]. Medscape; c1994-2022. Available from: https://emedicine.medscape.com/article/826792-medication#3. Accessed 25 Oct 2022.
9. Schellack N, Gani T. An overview of muscle pain. S Afr Pharm J. 2022;89(4):16-24 Available from: http://sapj.co.za/index.php/SAPJ/article/view/3113. Accessed 25 Oct 2022.

Prevention of rabies in humans

Published from the National Guidelines for the Prevention of Rabies in Humans, South Africa

V Essel,[1] J Weyer,[2] KJ Kabuya[3]

[1] Outbreak Response Unit, Division of Public Health Surveillance and Response, NICD

[2] Centre for Emerging Zoonotic and Parasitic Diseases, NICD

[3] Outbreak Response Unit, Division of Public Health Surveillance and Response, NICD

Driving progress towards rabies elimination: New WHO recommendations on human rabies immunization and results of Gavi's Learning Agenda on rabies & 2nd international meeting of the Pan-African Rabies Control Network (PARACON). Meeting Report, 12-14 September 2018, Johannesburg, South Africa. Geneva: World Health Organization; 2019. Licence: CC BY-NC-SA 3.0 IGO. Partially republished under the regulations of the Creative Commons Licence (CC BY-NC-SA 3.0 IGO) from https://apps.who.int/iris/.

S Afr Pharm J 2022;89(6):25-29

Rabies in humans

See Annexure 1 for a quick guide to human rabies.

Epidemiology of rabies in humans

Human rabies has predominantly been reported from KwaZulu-Natal, Eastern Cape, Mpumalanga, Free State and Limpopo provinces. In the past ten years, an average of 10 human cases (range 1–17) have been reported in SA per year. In 2018, 16 confirmed cases of human rabies were diagnosed from the following provinces: KwaZulu-Natal (n = 8); Eastern Cape (n = 6), Mpumalanga (n = 1) and Free State (n = 1). Figure 2 illustrates the distribution of laboratory-confirmed human rabies cases in SA from 2008–2018. Note how the distribution of human rabies cases overlaps with the distribution of canine (or domestic dog) cases presented in Figure 1.

Transmission to humans

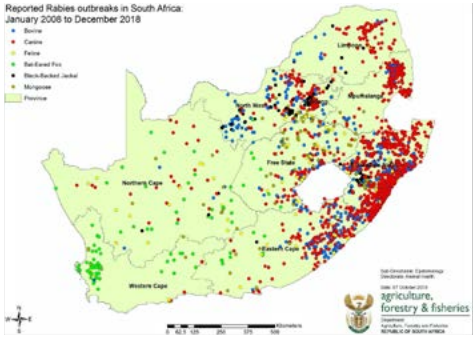
The rabies virus is transmitted to humans through virus-laden saliva from a rabid animal. The virus is shed in the saliva of an infected animal, which often hyper-salivates in response to infection, and can be introduced into another body through bites, scratches and any other wounds that transect the skin. Contact of the infected saliva with mucous membranes is also thought to be a possible route of infection, whereas contact of infected saliva with intact skin is not considered an exposure. Human cases are most often linked to exposures to rabid domestic dogs and few cases involving domestic cats or wildlife species have been reported.

Human-to-human transmission of the virus has been infrequently reported and has been limited to a few cases involving organ and graft transplantation from donors who have died of undiagnosed rabies. Although rabid patients may inflict bites and scratches on healthcare workers, no secondary cases of human rabies have been confirmed or reported following such exposures. The transmission of rabies virus through ingestion has also not yet been reported. This includes the ingestion of meat products or raw milk from confirmed rabid animals. The slaughtering with possible contact of spinal cord, brain and saliva should however be considered for potential risk of exposure to the virus.

Clinical presentation, diagnosis and treatment in humans

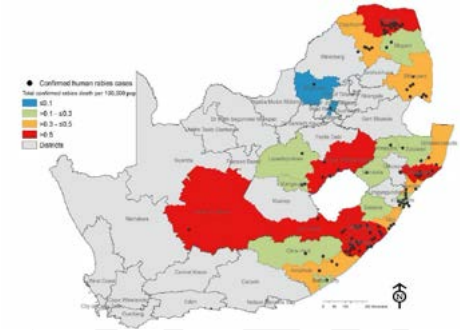
Rabies is fatal upon clinical presentation of the disease, so the focus is on preventing the disease by managing possible exposures to the virus.

The incubation period for the rabies virus (i.e. the period after exposure and before the appearance of signs and symptoms of the disease) varies, but is typically found to be between 20 and 90 days. Rare cases have been associated with shorter or longer incubation periods. During this period, very little (often nothing)



Please scan QR code to view original image

Figure 1: Geographical distribution of laboratory-confirmed cases of animal rabies in SA, 2008–2018. The canine cases include cases reported in domestic dogs (Map courtesy of DALRRD)



Please scan QR code to view original image

Figure 2: Geographical distribution of laboratory confirmed cases of human rabies in South Africa, 2008–2018 (Map courtesy of NICD)

Table I: Summary of PrEP regimen for rabies vaccines available in SA

Product name	Dosage	Site of administration	Schedule
i. Verorab™	0.5 ml (per vial) For intramuscular, full vial For intradermal, 0.1 ml per dose	Intramuscular: deltoid muscle in adults **OR** Intradermal*: 1 dose per site, 2 sites per day Intradermal sites: deltoid muscle, anterolateral thigh or supra scapular region	**Intramuscular:** One dose each on days 0 and 7 **Intradermal:** Two doses each on days 0 and 7
ii. Rabipur™ *Note: This product is currently not available in SA*	1.0 ml (per vial) For intramuscular, full vial For intradermal, 0.1 ml per dose		

*The intradermal schedule is recommended when PrEP is applied to groups of individuals and a cost benefit would apply (i.e. a single vial represents multiple doses)

may be noted clinically, with few a patients complaining of paraesthesia (tingling or 'pins-and-needles' sensation) and/or pain at the original wound site (or point of entry of the virus in the body). These paraesthesia-like symptoms are more commonly noted when symptoms of clinical rabies commence. In addition to the lack of signs and symptoms of illness during the incubation period, there are no laboratory markers or tests to confirm whether or not an individual has been infected with the rabies virus. The incubation period is followed by the onset of clinical symptoms, which is irreversible. Nearly two-thirds of patients develop furious rabies, which may include the following signs: hyperexcitability, generalised arousal, hydrophobia, aerophobia, aggression, confusion, etc. The remaining cases present with the paralytic form, which is not unlike Guillain-Barré syndrome. Most patients succumb within a week of the onset of symptoms. Even within an intensive care setting, survival rarely exceeds one month.

Clinical diagnosis is based on the observation of progressive encephalitis in a patient without an alternative confirmed diagnosis. Differential diagnoses for rabies include bacterial/viral meningitis (for example herpes virus infection, arboviral disease), cerebritis or encephalitis (such as cerebral malaria, trypanosomiasis), acute flaccid paralysis (for example poliomyelitis), but also non-infectious causes such as snake bite and psychosis. An epidemiological link involving possible exposure to a rabid animal (for example a dog bite) will strengthen the suspicion of rabies, but such histories are not forthcoming in all cases. There are no informative markers or blood screens that can be investigated to support the diagnosis of rabies. Magnetic resonance imaging may provide some insights, especially for differential diagnoses of other encephalopathies; computed tomography is typically normal and electroencephalography usually shows diffuse slow-wave activity. Specialised laboratory tests for rabies are always required to confirm or exclude the diagnosis. Ante-mortem diagnosis hinges on the detection of viral RNA in saliva, cerebrospinal fluid and/or nuchal biopsies (visit NICD website for more information, www.nicd.ac.za). However, the gold standard for rabies diagnosis remains the detection of rabies virus antigen in post-mortem collected brain specimens. The direct fluorescent antibody test is widely used for the diagnosis of rabies in animals and in humans, although other tests, such as the direct immunohistochemical test, have also been described for this purpose (visit NICD website for more information).

Pre-exposure prophylaxis for rabies

Rabies pre-exposure prophylaxis (PrEP) is recommended for individuals at high or continual risk of exposure to the rabies virus as defined by the WHO.[1] Individuals that may be predisposed for exposure to the rabies virus i) due to their occupation (such as veterinarians, other veterinary health professionals, animal welfare workers and laboratory workers), or ii) due to their hobbies such as bat enthusiasts or spelunkers, or iii) due to travel to canine rabies endemic areas where it is expected that rabies PEP may not be accessible if an exposure may occur and/or if particular activities undertaken during the travel will specifically predispose the traveller to possible exposure. The risk for rabies exposure for (ii) and (iii) is assessed on a case-by-case basis.

See Annexure 2 for the 'Prevention of human rabies' poster.

Regimen for rabies vaccine administration

Intramuscular administration of PrEP

The 2018 WHO position paper on rabies recommends the reduction of PrEP schedule to a two-day regimen administered via the intramuscular (IM) route (i.e. days 0 and 7).[1] See Table I.

Intradermal administration of PrEP

The WHO recommends intradermal (ID) vaccination as a safe and effective alternative to IM vaccine administration. In order to realise the cost benefit due to dose sparing associated with ID vaccination, it is recommended that PrEP be administered where groups of individuals (any group of people of two or more, such as a team of veterinarians or a travel group) will receive PrEP at the same time. For example, one vial containing 1.0 ml (0.5 ml) dose of vaccine, could ideally be used for up to 10 (5) intradermal doses of vaccine. See Table I.

Special considerations

Immunocompromised individuals

Individuals with documented immunodeficiency, such as symptomatic HIV infection, should be evaluated on a case-by-case basis and should receive a complete course of PrEP for immunocompromised individuals: a 3-visit rabies vaccine given either ID (2-sites) or IM (1-site) on days 0, 7 and the third dose given between days 21–28. In the event of possible exposures, full post-exposure prophylaxis (PEP) should be provided as described, including the IM schedule of four doses of vaccine and rabies immunoglobulin (RIG) therapy.

Pre-exposure vaccination boosting

It is recommended that individuals at high or continual risk for rabies exposure monitor vaccine-induced rabies immunity by testing rabies antibody titers (see next section). Pre-exposure vaccination boosting is recommended based on the outcome of the serological testing.

Laboratory testing of antibody titres in vaccinated individuals

Laboratory testing for post-vaccine rabies antibody titres is available in South Africa. Testing of antibody titres is recommended in order to determine if a pre-exposure booster is required to maintain an adequate level of immunological memory to support PEP responses in the event of an exposure. The frequency of testing is based on an assessment considering the risk of exposure to the rabies virus. The WHO recommends testing of antibody levels every two years for individuals such as veterinarians that are at high and continual risk of exposure.[1]

PEP is required in the event of exposure to the rabies virus, regardless of the antibody titre induced by PrEP.

Should a potential rabies exposure occur more than 3 months after a PreP course, rabies vaccine booster doses must be administered.

Note: Changes in the route of administration (IM vs ID) during the same PrEP course are acceptable, if unavoidable, to ensure complete PrEP course.

References

1. World Health Organization. Rabies vaccines: WHO position paper – April 2018. Available from: http://www.who.int/entity/rabies/resources/who_wer9316/en/index.html. Accessed 15 Aug 2020.

ANNEXURE 1: RABIES QUICK REFERENCE GUIDE

3 February 2021

RABIES

Quick reference guide

Rabies is 100% fatal but 100% preventable in humans with prompt and complete post-exposure prophylaxis (PEP). All animal exposures must be assessed for potential rabies virus exposure and whether rabies PEP is required. Rabies PEP consists of a course of rabies vaccine and rabies immunoglobulin (RIG), if indicated. All wounds have to be immediately washed and flushed for approximately 15 minutes using water, or preferably soap and water.

Delayed presentation

Rabies PEP should ideally be provided as soon as possible after exposure. If the patient presents well after the exposure event, consider the first day of presentation as day 0 for the administration of RIG and vaccine. If the wounds have healed, RIG can be infiltrated into and around previous wound sites.

If RIG is not available at the time of presentation

If RIG is not available at first visit, it should be sourced as a matter of urgency; however, its use can be beneficial up to seven days from the date of the first vaccine dose. The vaccine-induced immune response will be effective after seven days.

Multiple wounds

RIG must be infiltrated into every wound. If needed, dilute the RIG with normal saline to ensure sufficient volume to infiltrate all the wound areas.

Missed doses

Should a vaccine dose be missed for any reason, the PEP regimen should be resumed (not restarted), adhering to the minimum intervals between doses.

Immunocompromised individuals

Individuals with documented immunodeficiency, such as symptomatic HIV infection, should be evaluated on a case-by-case basis and receive a complete course of PEP including RIG. Irrespective of category of exposure or previous vaccination history, RIG and four doses of rabies vaccine should be administered, one on each day of days 0, 3, 7 and any day between day 14 and 28.

Wounds on high-risk sensitive areas

Wounds on the face, eyelid, scalp, ear and similar sensitive areas pose a challenge for local administration, especially in children. All wounds on the face are high-risk and rabies disease may develop after a short incubation period. It is **CRITICAL** in these cases that RIG is infiltrated **INTO THE WOUNDS.**

Where to give RIG for mucosal splashes

In case of mucosal exposures without a wound, rinse the area thoroughly with water, active immunisation with a vaccine course is recommended. Lavage of the area with RIG has been used but this is not an evidence-based recommendation.

Pregnant and lactating women

Rabies vaccine and RIG are safe and effective in pregnant and lactating women, and should be given if indicated. The dose is the same as for a non-pregnant adult.

Consumption of raw meat and milk from a rabid animal

No case of human rabies resulting from the consumption of raw meat from rabid animals has been documented. The rabies virus has never been isolated from milk of rabid cows and no documented human rabies case has been attributed to consumption of raw milk.

ANNEXURE 2: Prevention of rabies in humans

Also available from NICD website: www.nicd.ac.za

PREVENTION OF RABIES IN HUMANS

RABIES IS 100% FATAL BUT 100% PREVENTABLE IN HUMANS
WITH PROMPT AND COMPLETE POST-EXPOSURE PROPHYLAXIS (PEP)

RABIES EXPOSURE RISK ASSESSMENT

- All animal exposures must be assessed for potential rabies virus exposure and whether rabies PEP is required.
- Risk assessment is based on behaviour and health status of the animal, animal species, and geographical area where the exposure took place. Vaccination history of the animal may be unreliable, if in doubt, provide PEP.
- High risk rabies incidents may include: unprovoked animal attack; animal with unusual behaviour e.g, domestic animals becoming aggressive and wild animals appearing 'tame'; sick animal e.g, drooling, wobbling/unsteady gait, snapping at imaginary objects, and/or animal having died within 2 weeks after the human attack.
- Rabies is not transmitted by birds or reptiles. Low risk species in South Africa (RSA) include mice, rats, squirrels, monkeys and baboons.
- Do not delay PEP pending laboratory confirmation of rabies in an animal – PEP may be discontinued if results are negative for the animal involved.

MANAGEMENT OF PATIENT

General wound management is critical in all patients:

- Flush well with soap and water for at least 5 - 10 minutes, then clean with chlorhexidine solution (0.05%). Disinfect with iodine solution/ointment.
- Avoid or delay suturing (where possible) and use of local anesthetic agents (may potentially spread the virus locally).
- Provide antibiotics (e.g. amoxicillin clavulanate) and/or tetanus vaccination as required.

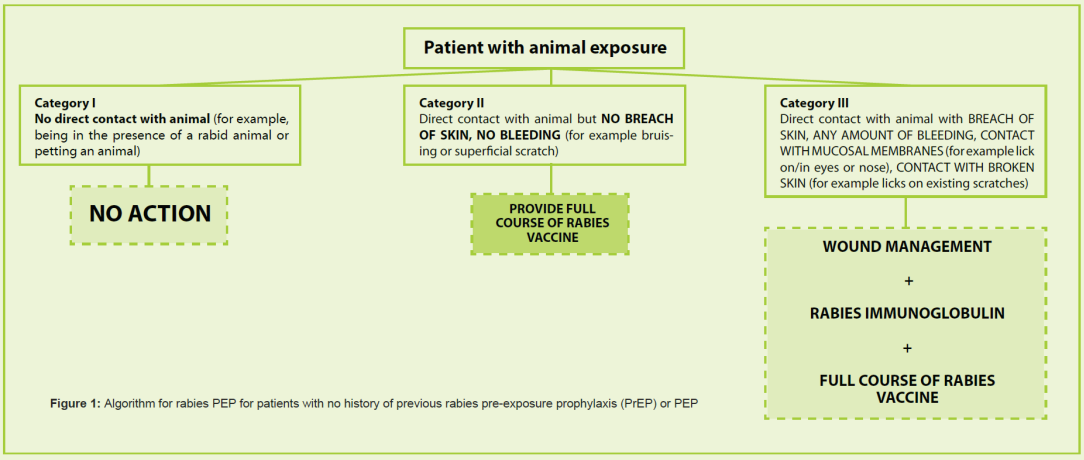


Figure 1: Algorithm for rabies PEP for patients with no history of previous rabies pre-exposure prophylaxis (PrEP) or PEP

RABIES VACCINE

- Vaccination schedule requires FOUR doses.
- Course: days 0, 3, 7 and any day between day 14 and 28 (Day 0 = day of first vaccination).
- Intramuscular injection in deltoid muscle in adults, anterolateral thigh in small children (< 2 years of age). INEFFECTIVE IF GIVEN IN GLUTEUS MAXIMUS (Buttocks).
- Dose: 1 vial equals one dose (regardless of vial size) for adults/children.

RABIES IMMUNOGLOBULIN (RIG)

- Dose: 20 IU (human derived RIG products) or 40IU (equine derived RIG products) per kilogram of body weight (i.e. calculate for each case). Infiltrate RIG in and around wounds, giving as much as anatomically possible without compromising blood supply (especially for extremities).
- Evidence has shown that maximum infiltration of RIG in and around the wound is effective and that there are no benefits from additional intramuscular administration of any remaining RIG at a site distant to the wound.
- If multiple wounds, dilute RIG in equal volumes of saline and infiltrate all wounds.
- Different strengths/preparations for the RIG products are available. Check the package insert of all RIG products to ensure that the right dosage and volume is administered.
- RIG provides immediate immunity and is administrated as soon as possible but not beyond 7 days after administration of first dose of vaccine (for example, if not available at clinic, needs to be urgently sourced).

SPECIAL CONSIDERATIONS

- **Immunocompromised**: Symptomatic HIV infection or other documented immunodeficiency, in category II and III exposures, provide full course of vaccine and RIG, regardless of previous rabies vaccination history.
- **Pregnant women & children**: No contraindication to vaccine or RIG.
- **Individuals who have been vaccinated for rabies before**: No RIG required. For PEP, give booster vaccination (course: days 0 and 3) (irrespective of pre-exposure vaccination antibody titer).
- **Individuals at high or continual risk for rabies exposure (such as veterinarians)**: Provide pre-exposure vaccination comprising 2 doses of vaccine (Course: days 0 and 7, 21 or 28). Monitor antibody over time through serological testing.

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

MORE INFORMATION:
NICD website: www.nicd.ac.za
NICD Hotline for Clinical Advice: 082 883 9920
Updated: SEPTEMBER 2021

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Adapted from: Rabies vaccines; World Health Organization Position Paper - April 2018. Available from http://apps.who.int/iris/bitstream/handle/10665/272371/WER9316.pdf?ua=1

APSSA Annual Conference 21–23 August 2022

Prof. Sandile Khamanga
Conference convener


Prof Sandile Khamanga

The Academy of Pharmaceutical Sciences (APSSA) held their 41st annual conference and 43rd Annual General Meeting at Rhodes University in Makhanda (formerly Grahamstown) on 21–23 August 2022. The theme of the conference was 'Back to the Future", in reference to the return to in-person conferences and the face-to-face interactions with colleagues that so often sparks new ideas and collaborations. Since its inception in 1978, the APSSA conference has been well attended by pharmacists, and other colleagues, from the academic and industrial sectors. Unfortunately, due to the COVID-19 pandemic the annual conference was postponed in 2020 and 2021 as the restrictions did not allow for the social interaction vital to the conference. So, it was with great excitement that the Rhodes University Faculty of Pharmacy took up the challenge to host the first in-person conference since 2019.

The conference commenced on Sunday 21 August with a function at which the Rhodes University DVC: Academic and Student Affairs, Professor Monnapula-Mapesela, welcomed all to Rhodes University and commented about the contentious theme and encouraged delegates to challenge the status quo in their area of research. The Dean of Pharmacy at Rhodes University, Professor Sandile Khamanga added his welcome and expressed his delight at the fact that there were many young scientists attending this conference for the first time. A variety of presentations from academic pharmacists and postgraduates were delivered over the following two days. Their talks, and the interactive Q+A sessions, gave valuable insight into the latest academic research taking place in pharmacy. Overall, the programme was very successful with 13 posters, 16 Young Scientist presentations and 23 podium presentations.

The academic proceedings commenced with a plenary lecture delivered by Professor Piotr Lulinski, Deputy Dean of the Faculty of Pharmacy at the Medical University of Warsaw. He eloquently espoused the potential role of molecularly imprinted polymers as novel drug delivery technologies in his well-received presentation.

Dr Ralph Tettey-Amlalo delivered an invited presentation in which he shared the journey of producing a complementary medicine using indigenous natural sources, whilst complying with stringent regulatory hurdles to ensure standardisation from seed to product was achieved. Encouragingly, he suggested this was an opportunity for the development of future products.

Professor Sarel Malan had an interesting and enlightening presentation on INN stems for naming of compounds. He also shared several online resources that are available from the WHO for information and suggested their use in teaching and learning of pharmacology and clinical pharmacy may enhance learning outcomes.

Professor Rod Walker delivered a presentation in which he shared the story of the hand sanitiser production project that was undertaken during the COVID-19 pandemic project and for which he received the Distinguished Vice-Chancellors Community Engagement Award. Professor Walker challenged pharmacists in the delegation to use their professional expertise and skills in a forward-thinking manner.

The Young Scientists component of the conference allowed Young Scientist delegates to give ten-minute presentations on their work to the delegates and to a panel of judges. This format required projects to be concisely and clearly presented, which can be considered a challenging task. However, it was rewarding for the presenters to be able to share their work both with their peers and mature researchers. The standard of submitted abstracts and posters and the presentations was high. Sandrine Tanga (UWC) and Maxine Grose (Wits) were well deserving of the Young Scientist prizes.

Exhibitors displayed their promotional materials and introduced academics to their newest products and services, finding the conference platform an excellent opportunity to reach the largest assembling of participants from the pharmacy academic field.

As in the past, the social programme permitted interaction with exhibitors and colleagues at teas, meals and between sessions. The pub quiz evening and gala dinner were particularly enjoyed by delegates. During the gala dinner, the Young Scientist, Best Publication, Best Poster, Best Oral Presentation and Teacher of the Year awards were presented.

The all-inclusive registration fee supplemented by generous sponsorship support, allowed delegates to be accommodated in student residences and have all local transport, meals and social events covered. The overall cost per person was affordable and encouraged universities to send as many delegates as possible.

Delegates shared extremely positive and encouraging feedback on the conference experience. One of the highlights expressed was the participation of almost all universities that offer Pharmacy. Networking opportunities were also a highlight for many staff and students who were attending the conference for the first time.

The conference also hosted the 43rd AGM of the Academy, which had been held in virtual format in 2020 and 2021. We congratulate the following members who will serve on the 2022–2024 Executive Committee:

Prof. Varsha Bangalee (UKZN)

Prof. Yahya Choonara (Wits)

Prof. Sandile Khamanga (Rhodes)

Dr NomaChina Kubashe (NMU)

Prof. Lesetja Letsoane (NWU)

Prof. Kenechukwu Obikeze (UWC)

Ms Lorraine Thom (SMU)

Dr Ilze Vermaak (TUT)

Participating in the 41st annual conference was exciting, motivational, and made all of us enthusiastic about next year's APSSA conference which will be hosted by UKZN. It also made us appreciate the value of the in-person conference experience and how this format is an invaluable tool for networking, learning, and innovation.

We thank everyone for participating and supporting the conference to make it the great success that it was.

Awards

Aspen Pharmacare Young Scientist Winner – Laboratory Sciences

Sandrine Tanga (UWC)
Design of a thermoresponsive hydrogel for enhanced intratumoral permeation of a model drug in oral squamous cell carcinoma biosuture

Aspen Pharmacare Young Scientist Winner – Practice

Maxine Grose (Wits)
Diabetic foot ulcers: Is it time to readdress the standard treatment guidelines

Distinguished Teacher of the Year

The 2022 winner was Ané Orchards from the University of the Witwatersrand.

Publication Awards

Pharmaceutical Chemistry
Ayodeji Egunlusi (UWC)
Open and rearranged norbornane derived polycyclic cage molecules as potential neuroprotective agents through attenuation of MPPþ- and calcium overload-induced excitotoxicity in neuroblastoma SH-SY5Y cells

Pharmaceutics
Yahya Choonara (Wits)
Development of a fluid-absorptive alginate-chitosan bioplatform for potential application as a wound dressing

Pharmacology
Gill Enslin (TUT)
Anti-seizure activity of African medicinal plants: The identification of bioactive alkaloids from the stem bark of Rauvolfia caffra using an in vivo zebrafish model

Pharmacy Practice
Sandy van Vuuren (Wits)
Laboratory-based study of novel antimicrobial cold spray coatings to combat surface microbial contamination

Oral presentation

Winner – Stephanie Leigh de Rapper (Wits)
Runner-up – Richard Beteck (NWU)

Poster award

Winner – Keagile Lepule (TUT)
Runner-up – Weiyang Chen (TUT)

Sponsors

The APSSA would like to thank all the sponsors for their generous contributions:
Anatech
Chemetrix
Lugaju Innovations
Phed Pharma Solutions
Rhodes University
Separations

Courage to change

Kaajal Chetty
President, SAAHIP

Change is inevitable but personal growth is a choice" … Bob Proctor

Keeping the above quote in mind, one can view change as either good or bad as it all depends on *your* intent and outlook. Our environment may throw many hurdles or opportunities our way. It is up to us how we embrace the change necessary for happiness and fulfilment. The other question we must ask is: "Do we wait for the world to change to suit us or do we change ourselves to adapt and thrive?"

Kaajal Chetty

A very personal story of mine is my decision to study pharmacy. Alas, there was no great calling or focus, just an inclination towards doing something to actively help people. Also, persuasion from a relative to enter into the field and not take a gap-year.

Moving from first to second year of university, I slowly felt the pressure and enormity of the subjects. A friend and I even joked that we would change over to *engineering* if we failed the year. I was still very much 'on the fence' about this whole *pharmacy* thing.

And then came 'Pharmacy Practice'… a subject that took me into the real-life workings of the profession. Providing me with insight and helping me develop in that professional role. Changing my mind and perspective on the importance of the pharmacist. Gone were the jokes about changing career paths. I had found my place and developed the greatest *respect* for the profession.

Making a change for the wrong reason in this case could have steered me down a completely different path. Away from what I now believe to be my destiny. My pharmacy journey thus far has been exciting and enriching, mostly a comedy-drama and sometimes an action-thriller.

My time with SAAHIP has truly been an epic adventure. This profession has led me to meet many wonderful pharmacists, make the best of friends, and grow both professionally and personally.

Our personal journey to our profession will differ, but I hope that we share the respect for it and value its worth. Understanding what you do and knowing how it fits into the grand picture of optimal patient care can be a great driving force. I love being a pharmacist, having the potential to change things for the better, and I respect the power I have been given as a healthcare professional to care for my patient.

The Society and its sectors empower us to grow and develop the field. To have a say, to bring about the change that we want to see in the world. Being a member of PSSA allows us to step into the role of guardian of the profession and to make well-informed decisions.

And so, back to my personal story…

I have practised in the private and public hospital sectors for almost 15 years. I have happily devoted over 8 years of my spare time (and sleep) to SAAHIP and now I find myself at another changing point. After the shortest presidency in SAAHIP history, I will be starting a new journey as the PSSA Director of the Cape Western Province branch. My journey with SAAHIP National seems somewhat incomplete but I will be around, in a different position but always cheering the Association on. I look forward to this change in role and I am excited for the adventure ahead.

Our generation may one day rule the population, but we need to be brave enough today to step forward and take an interest in our profession. We want to leave this world a better place and live a life that matters. These goals may require you to get out of your comfort zone. So when the world calls for it… do you have the courage to change?

Medication without harm: "know, check, ask, record and report"

Nirupa Misra,[1] Kaajal Chetty[2]

[1] Pharmacy Manager, King Dinuzulu Hospital Complex, South Africa

[2] Mahatma Gandhi Memorial Hospital, South Africa

Introduction

Unsafe care, leading to patient harm, is a global public health challenge. It is estimated that 134 million adverse events due to unsafe care occur in hospitals in low- and middle-income countries, contributing to about 2.6 million deaths every year.[1] Medications are the most widely used interventions in health care, and medication-related harm constitutes the greatest proportion of the total preventable harm due to unsafe care. In addition, such harm results in economic and psychological burdens to patients and society. Much of this patient harm is avoidable. As countries strive to achieve Universal Health Coverage and the Sustainable Development Goals, the beneficial effects of improved access to health services can be undermined by unsafe care. Patient safety incidents can cause death, disability and suffering for victims and their families and may result in reduced public confidence and trust in local health systems.

In 2019, the 72nd World Health Assembly adopted Resolution WHA72.6 on global action on patient safety.[2] The resolution urges Member States to recognise patient safety as a health priority. The World Health Organization (WHO) launched its third global patient safety challenge – "Medication Without Harm" – in 2022. The goal is to reduce severe, avoidable harm related to medicines by 50% in the next 5 years, by empowering patients, their caregivers and healthcare professionals to take an active role in ensuring safer medication practices and medication use processes. Pharmacists are well placed to educate and advise patients on the correct use of their medicines and to strengthen pharmacovigilance (PCV).

Pharmacovigilance

PCV is defined by WHO as "the science and activities relating to the detection, assessment, understanding, monitoring and prevention of adverse effects or any other drug-related problem".[3] Vigilance therefore means the continuous monitoring and evaluation of the safety, efficacy and performance profile of any medicine, medical device or in vitro diagnostic, and the management of any risk throughout its life-cycle. An adverse drug event is defined as any response to a medicine which is noxious (harmful or unpleasant) and unintended which occurs at doses used in man for prophylaxis, diagnosis or to treat. Where an event is causally linked to the drug it is termed an adverse drug reaction (ADR). ADRs may arise due to different factors related to the medicine, the patient and processes of care. Predisposing patient factors may include age, coexistence of other diseases, allergies, overlapping toxicities, pharmacogenetic susceptibility and pregnancy. Drug administration errors may also contribute to patients presenting with an ADR.

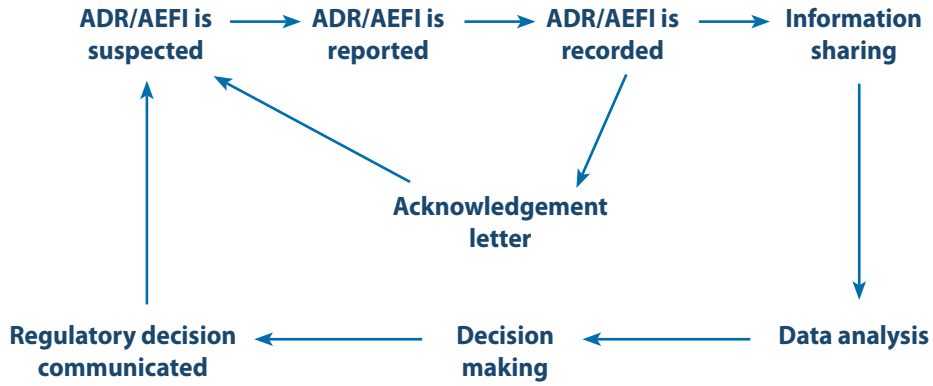
ADRs can be classified in several ways. Severity is a subjective assessment made by the patient and/or the healthcare professional of the intensity of an event and relates to its impact on the patient's activities. Severity is often classified on a three-point scale from "mild" through "moderate" to "severe", commonly on the basis of a clinician's judgement. In clinical trials, a grading system is sometimes used. ADRs can also be classified based on their time of onset, as dose-related or non-dose-related, as cumulative, or after withdrawal. Unexpected failure of therapy can also be regarded as an ADR.

Although spontaneous, voluntary reporting of suspect adverse reactions during routine clinical practice can be considered a passive method, it has value in the early detection of patient safety issues. Targeted spontaneous reporting (TSR) targets challenged or new areas (such as drug-resistant tuberculosis).[4] It is particularly important to consider when critical information that may impact on policy or clinical treatment regimens is not reaching the regulatory authority on time. Active surveillance requires that patients are asked directly or patient records are screened to detect adverse events. With new anti-tuberculosis medicines and novel regimens for drug-resistant tuberculosis, active drug safety monitoring and management (aDSM) has been implemented.[5] This is the active and systematic, clinical and laboratory assessment of patients on treatment, to detect, manage and report suspected or confirmed drug toxicities.

Vaccine PCV consists of the activities for the detection, assessment, understanding and communication of "adverse events following immunisation" (AEFI) and other vaccine- or vaccination-related issues and the prevention of untoward effects of vaccines or vaccination. AEFI is defined as any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. Thus, a reported adverse event does not automatically mean that it was caused by the vaccine. WHO have defined five cause-specific AEFI, which differentiate vaccine- and vaccination-related reactions from coincidental events by rigorous assignment of causality:

Reaction to a vaccine product: caused or precipitated by one or more of the inherent properties of a vaccine;

- **Reaction to a defect in vaccine quality**: caused or precipitated by one or more defects in the quality of a vaccine, including its administration with a device provided by the manufacturer;
- **Reaction to an immunisation error**: caused by inappropriate handling, prescribing or administration of a vaccine;
- **Reaction related to anxiety**: arising from anxiety about immunisation; and



The SAHPRA guidelines outline the process followed when an ADR is reported

- **Coincidental event**: caused by something other than a vaccine, immunisation error or immunisation anxiety.[6]

The need for ongoing pharmacovigilance

Although safety is a key component of the drug development process, addressed from preclinical animal studies to clinical trials, there are notable gaps in the data available at the time of registration of a new medicine. Clinical trials are conducted in a controlled environment, in relatively small number of patients, with strict inclusion and exclusion criteria, and usually for a short duration. The goal of PCV is to safeguard public health and improve rational use of medicine through efficient and timely collection of safety information, assessment and communication of risks and benefits, in order to support local decision-making. Pharmacists should be the champions of PCV ensuring the medicine does not cause harm.

Adverse events can be reported by patients or any healthcare worker, including traditional healers and manufacturers. Reporting should be confidential and the patient/organisational information must be kept secure. An ADR report does not constitute an admission of liability or that the health professional contributed to the event in any way. Every problem related to the use of a medicine, including vaccines, drugs used in traditional medicine, herbal remedies, cosmetics and medical devices should be reported. All serious and non-serious suspected adverse reactions (expected or unexpected), suspected ADRs associated with drug-drug, drug-food, drug-herbal interactions and suspected ADRs associated with drug withdrawal should be reported. Lack of efficacy, ADR associated with overdose or medication errors, counterfeit pharmaceuticals, product quality issues, development of resistance and treatment failure should also be reported.

ADR reporting can be done manually by completing the PCV form, which can be submitted by email (adr@sahpra.org.za), or electronically, via the Med Safety app (https://medsafety.sahpra.org.za/). More details can be obtained in the South African Health Products Regulatory Authority (SAHPRA) guidelines.[6]

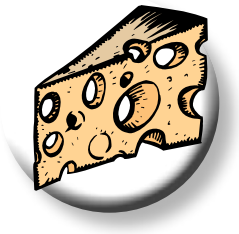
Apart from contributing to the quality of ADR reports, by screening for completeness, pharmacists can also contribute by fostering discussion in local structures, such as Pharmaceutical and Therapeutics Committees. Meetings of such multidisciplinary teams can review ADR reports generated at the facility and also perform causality assessments, using the WHO Upsala or Naranjo Causality Assessment tools. However, all reports should be submitted, not only those which are considered to be causally linked. Feedback received from the regulatory authority can also be discussed at facility level, which may trigger actions to improve the safe use of medicine.

Conclusion

PCV contributes to patient care and aims at getting the best outcome from treatment with medicines. Good PCV practice will identify emerging risks within the shortest possible time after the medicine has been marketed and will help to establish or identify risk factors. Such information will ultimately help each patient to receive optimum therapy at a lower cost to the health facility. Developing the right expertise, capacity building and mentorship are important in ensuring detection and management of ADRs, recording and reporting. Pharmacists play an integral role as part of the healthcare team to ensure the safe use of medicine.

References

1. World Health Organization. Global patient safety action plan 2021–2030: towards eliminating avoidable harm in health care. Geneva: World Health Organization; 2021.
2. World Health Assembly. Resolution 72.6: Global action on patient safety. Geneva: World Health Organization; 2019.
3. World Health Organization. Available from: https://www.who.int/teams/regulation-prequalification/regulation-and-safety/pharmacovigilance. Accessed 9 Sept 2022.
4. World Health Organization. A practical handbook on the pharmacovigilance of medicines used in the treatment of tuberculosis. Enhancing the safety of the TB Patient. Geneva: World Health Organization; 2012.
5. World Health Organization. Active tuberculosis drug-safety monitoring and management (aDSM). Framework for implementation. Geneva: World Health Organization; 2015.
6. World Health Organization. Immunization stress-related response. A manual for program managers and health professionals to prevent, identify and respond to stress related responses following immunization. Geneva: World Health Organization; 2019.
7. South African Health Products Authority. Guideline for adverse drug reactions (ADRs) reporting for healthcare professionals (SAHPGL-CEM-PV-06). Available from: https://www.sahpra.org.za/wp-content/uploads/2022/08/SAHPGL-CEM-PV-06-v2_Adverse-Drug-Reactions-ADRs-Reporting-for-Healthcare-Professionals.pdf. Accessed 9 Sept 2022.



Pharmstory
"A Pharma makes a plan!"

Gary Black

Having grown up in a "*platteland dorpie"* and spent much time on my friends' farms, I for one, am very familiar with the well-known idioms, *"n Boer maak 'n plan!"* and "*Daar is niks wat 'n boer nie kan regmaak met 'n tang en 'n stukkie bloudraad nie!"* I personally witnessed how anything from fences, bucket handles, gate/door hinges, windmills, wagons and tractors were skilfully repaired this way and held together securely until the next visit to the "*ko-op*" in town when the requisite hinge, screw, bolt or engine part could be bought. While such innovation was born out of desperate necessity, those circumstances required entrepreneurial thinking and engendered a positive spirit of *"Never say die!"*

In the 1950s and 60s, my father, the only pharmacist in the "*dorp",* found himself in similar circumstances. He had adopted a philosophy that if anyone in the district, from the poorest to the richest, the uneducated to the most highly qualified, irrespective of colour, creed, culture or religion, needed advice on medicine, he, their pharmacist, should be their first port of call. Those were the days before mass production and marketing of medicines and the local community relied heavily on their pharmacist to use his unique knowledge of medicine and formulation to dispense just the right mixture for their particular medical condition. Medicines were considered individualised treatments for the patients who required them, as opposed to, sadly, the recent trend of commercialisation of medicines and corporatisation of pharmacies where medicines are deemed to be just another commodity and patients are treated as mere consumers.

In those days, having successfully completed his studies and apprenticeship, a pharmacist was registered as a "*Chemist and Druggist*". Pharmacists were recognised by the community, not only for their ability to compound and dispense suitable medicines, but also for their knowledge of chemistry. The pharmacist was the person to turn to when a problem requiring some knowledge of chemistry arose, and so, like his farming colleagues, the pharmacist *"had to make a plan!"* While he may not have been adept at using a *"tang and bloudraad"* he certainly could formulate and compound mixtures for solving any number of problems. Cosmetic, toiletry and hair preparations, pursuant to human vanity, were top of the list of requests. More effective cleaning materials (especially stain removers), polishes, lacquers and adhesives and other household requirements were always being sought by local housewives and craftsmen. *"Plattelanders"* are usually proud gardeners so there was a demand for horticultural preparations such as pesticides, insecticides and fertilisers. There was not a vet within 100 km, so, any number of veterinary formulas were also called for.

A number of older colleagues may be familiar with the reference books "*Pharmaceutical Formulas Vol I and II".* Volume I contained formulae of medicinal preparations, while Volume II those of other preparations such as mentioned above. These books are aptly sub-titled *"The Chemist's Recipe Book"* and were published by "*The Chemist and Druggist*" at their offices in London. The first edition appeared in 1898 and publication continued into the 1950s. Earlier editions appeared as a single volume and it was from the 10th edition in 1929 that the work was split into two volumes. There is no doubt that "*Pharmaceutical Formulas*" served as an important reference for the formulation of the many different remedies that the local "*Chemist*" was called on to prepare. However, pharmacists of that era usually devised their own formulae which were carefully recorded in their own "*little black book*". Many of the remedies first prepared in the dispensary of a "*platteland apteek"* went on to become commercially well-known household names, "*Nervepain Specific*" and "*Clock Tower Ointment*" being two such products.

When the commercially available lotions, creams and potions did not live up to their advertised promises, most people, being the vain creatures that they are, called on the local pharmacist with his special knowledge of chemistry and medicine to devise the miracle formula required. One such case involved a relatively young man who shall be known simply as John. In the late 50s and early 60s (even before the Beatles and Rolling Stones) rock-'n-roll reigned supreme. Plenty of make-up, curled and teased hair for the girls meant good business for the local pharmacy while the young men strived to emulate the likes of Buddy Holly, Bill Haley, Ricky Nelson and, of course, Elvis Presley. A hairstyle like that of Ricky Nelson, Cliff Richard or Elvis was the ultimate goal for our secretly vain John. Now John, with his flat feet, chubby cheeks and portly body could never really compete with his younger rivals on the dance floor with their twisting legs and gyrating hips (in true Elvis style). He did, however, have a reasonable head of dark hair, which, although a little wavy, he obviously regarded as his best

physical asset. So John went about growing his hair a little longer in the hope of attaining a true Elvis-style coiffure. The problem was that the longer his hair grew, the wavier it emerged. No amount of *Brylcream, Trugel*, *Potter's Brilliantine* or even *La Pebra* could transform his black waves into the sleek straight strands he so desired.

So, of course, he confided his secret wish to Mr Black, the pharmacist, in a desperate hope that he could produce some unique solution to the problem. This set my father off on a journey of experimentation and formulation in pursuit of the magic potion that would tame John's head of wavy, black hair. Over the next few months, John was regularly seen to be consulting Mr Black confidentially in the confines of a closed dispensary, dutifully reporting on progress. After each such consultation there would be some adjustments to the formula until one day, *"Eureka*!" the perfect hair cream was achieved. My father was sworn to secrecy while John's new, improved look was admired around town! Although John never did win any talent or beauty competitions, he was a kind man and went on to win himself a bride from amongst the few eligible young ladies in the town, settled down to a steady job and raised a daughter of his own. I secretly like to think that the innovative formulation of just the right hair cream by Mr Black, the pharmacist, somehow played an important role in John's ultimate success with the ladies!

"Ja-nee Boet!" When "*a Pharma makes a plan*", shows empathy, uses his knowledge and the tools of his trade, he can really make a positive difference in the lives of his patients!

Ek sê maar net!

Multi-Tasking RAPID *Relief*

Ryaltris®

665 mcg
25 mcg

(olopatadine hydrochloride and mometasone furoate monohydrate nasal spray)

NEW registered indications for *Ryaltris®* Nasal Spray!

Ryaltris®

Now indicated for the symptoms associated with: [1]

- **Seasonal Allergic Rhinitis (SAR)**
- **Perennial Allergic Rhinitis (PAR)**
- **Rhinoconjunctivitis**

in patients ≥ 12 years of age

REFERENCE: 1. SAHPRA approved professional information. Date of revision: April 2022.

S2 RYALTRIS® (Nasal spray). Reg. no. 53/21.5.1/0457. Each spray delivers 600 µg olopatadine (as olopatadine hydrochloride) and 25 µg mometasone furoate (as mometasone furoate monohydrate). Contains the preservative benzalkonium chloride 0,02 % w/w. Sugar free. For full prescribing information refer to the professional information approved by the South African Health Products Regulatory Authority. Date of revision: April 2022.

HCR: Glenmark Pharmaceuticals South Africa (Pty) Ltd. 2nd Floor, Building D, Stoneridge Office Park, 8 Greenstone Place, Greenstone, Edenvale, Gauteng, 1609. (Office) +27 11 564 3900. www.glenmarkpharma.com. ZAR/06/2022/56

Glenmark
A new way for a new world

Glenmark, touching the lives of patients for over three decades.

Medpharm® Publications

MEDICAL AND PHARMACEUTICAL JOURNAL PUBLISHER

Founded in 1988, Medpharm Publications has a publications list of more than ten titles comprising of over fifty journal editions. With a reach of more than 40 000 healthcare workers countrywide (printed editions) and an established global audience.

WHAT MAKES OUR JOURNALS DIFFERENT?

- Academic medical journals that reach YOUR target market
- Official journal for the various related societies
- Official journal at society related congresses
- 11 medical journals to choose from
- Peer reviewed articles
- All journals available digitally www.medpharm.co.za
- Privately owned company (Directors: Prof. Oppel Greeff & Pierre Marais)

WWW.MEDPHARM.CO.ZA